This Agreement (‘the Agreement’) is between the following parties:

on the one part,

the European Union (‘the EU’), represented by the European Commission (‘the Commission’), represented for the purposes of signature of this Agreement by the Head of Unit, Directorate-General for Research and Innovation, Innovative Administration, Financial Management & Program Support II, Mila BAS SANCHEZ,

and

on the other part,

1. ‘the coordinator’:

UNIVERSITEIT ANTWERPEN (UANTWERPEN), established in PRINSSTRAAT 13, ANTWERPEN 2000, Belgium, VAT number: BE0257216482, represented for the purposes of signing the Agreement by Rector, Herman VAN GOETHEM

and the following other beneficiaries, if they sign their ‘Accession Form’ (see Annex 3 and Article 56):

2. INSTITUT PASTEUR (IP), established in RUE DU DOCTEUR ROUX 25-28, PARIS CEDEX 15 75724, France, VAT number: FR65775684897,

3. UNIVERSITAIR MEDISCHE CENTRUM UTRECHT (UMC UTRECHT), established in HEIDELBERGLAAN 100, UTRECHT 3584 CX, Netherlands, VAT number: NL004205315B01,

4. ERASMUS UNIVERSITAIR MEDISCHE CENTRUM ROTTERDAM (ERASMUS MC), established in DR MOLEWATERPLEIN 40, ROTTERDAM 3015 GD, Netherlands, VAT number: NL801427228B01,

5. THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD (UOXF), established in WELLINGTON SQUARE UNIVERSITY OFFICES, OXFORD OX1 2JD, United Kingdom, VAT number: GB125506730,

6. CHARITE - UNIVERSITAETSMEDIZIN BERLIN (CHARITE), established in Chariteplatz 1, BERLIN 10117, Germany, VAT number: DE228847810,
7. **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)**, established in RUE DE TOLBIAC 101, PARIS 75654, France, VAT number: FR31180036048,

8. **ACADEMISCH MEDISCH CENTRUM BIJ DE UNIVERSITEIT VAN AMSTERDAM (AMC)**, established in MEIBERGDREEF 15, AMSTERDAM 1105AZ, Netherlands, VAT number: NL004627672B01,

9. **FONDAZIONE PENTA - FOR THE TREATMENT AND CARE OF CHILDREN WITH HIV ANDRELATED DISEASES - ONLUS (PENTA)**, established in CORSO STATI UNITI 4, PADOVA 35127, Italy, VAT number: IT04150680280,

10. **INSTITUT PASTEUR OF SHANGHAI, CHINESE ACADEMY OF SCIENCES (IPS)**, established in SOUTH CHONGQING ROAD BUILDING 2 LUWAN DISTRICT 225, SHANGHAI 200025, China (People's Republic of), as ‘beneficiary not receiving EU funding’ (see Article 9),

Unless otherwise specified, references to ‘beneficiary’ or ‘beneficiaries’ include the coordinator.

The parties referred to above have agreed to enter into the Agreement under the terms and conditions below.

By signing the Agreement or the Accession Form, the beneficiaries accept the grant and agree to implement it under their own responsibility and in accordance with the Agreement, with all the obligations and conditions it sets out.

The Agreement is composed of:

**Terms and Conditions**

- Annex 1  Description of the action
- Annex 2  Estimated budget for the action
  - 2a  Additional information on the estimated budget
- Annex 3  Accession Forms
- Annex 4  Model for the financial statements
- Annex 5  Model for the certificate on the financial statements
- Annex 6  Model for the certificate on the methodology
TERMS AND CONDITIONS

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This Agreement sets out the rights and obligations and the terms and conditions applicable to the grant awarded to the beneficiaries for implementing the action set out in Chapter 2.

CHAPTER 2 ACTION

ARTICLE 2 — ACTION TO BE IMPLEMENTED

The grant is awarded for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response’ — ‘RECoVER’ (‘action’), as described in Annex 1.

ARTICLE 3 — DURATION AND STARTING DATE OF THE ACTION

The duration of the action will be 24 months as of 14 February 2020 (‘starting date of the action’).

ARTICLE 4 — ESTIMATED BUDGET AND BUDGET TRANSFERS

4.1 Estimated budget

The ‘estimated budget’ for the action is set out in Annex 2.

It contains the estimated eligible costs and the forms of costs, broken down by beneficiary (and linked third party) and budget category (see Articles 5, 6, and 14). It also shows the estimated costs of the beneficiaries not receiving EU funding (see Article 9).

4.2 Budget transfers

The estimated budget breakdown indicated in Annex 2 may be adjusted — without an amendment (see Article 55) — by transfers of amounts between beneficiaries, budget categories and/or forms of costs set out in Annex 2, if the action is implemented as described in Annex 1.

However, the beneficiaries may not add costs relating to subcontracts not provided for in Annex 1, unless such additional subcontracts are approved by an amendment or in accordance with Article 13.

CHAPTER 3 GRANT

ARTICLE 5 — GRANT AMOUNT, FORM OF GRANT, REIMBURSEMENT RATES AND FORMS OF COSTS

5.1 Maximum grant amount

The ‘maximum grant amount’ is EUR 4 995 820.00 (four million nine hundred and ninety five thousand eight hundred and twenty EURO).

5.2 Form of grant, reimbursement rates and forms of costs
The grant reimburses **100% of the action's eligible costs** (see Article 6) (‘reimbursement of eligible costs grant’) (see Annex 2).

The estimated eligible costs of the action are EUR **4,995,820.00** (four million nine hundred and ninety five thousand eight hundred and twenty EURO).

Eligible costs (see Article 6) must be declared under the following forms ('forms of costs'):

(a) for **direct personnel costs**:
   - as actually incurred costs (‘actual costs’) or
   - on the basis of an amount per unit calculated by the beneficiary in accordance with its usual cost accounting practices (‘unit costs’).

   Personnel costs for SME owners or beneficiaries that are natural persons not receiving a salary (see Article 6.2, Points A.4 and A.5) must be declared on the basis of the amount per unit set out in Annex 2a (unit costs);

(b) for **direct costs for subcontracting**: as actually incurred costs (actual costs);

(c) for **direct costs of providing financial support to third parties**: not applicable;

(d) for **other direct costs**:
   - for costs of internally invoiced goods and services: on the basis of an amount per unit calculated by the beneficiary in accordance with its usual cost accounting practices (‘unit costs’);
   - for all other costs: as actually incurred costs (actual costs);

(e) for **indirect costs**: on the basis of a flat-rate applied as set out in Article 6.2, Point E (‘flat-rate costs’);

(f) **specific cost category(ies)**: not applicable.

5.3 **Final grant amount — Calculation**

The ‘**final grant amount**’ depends on the actual extent to which the action is implemented in accordance with the Agreement’s terms and conditions.

This amount is calculated by the Commission — when the payment of the balance is made (see Article 21.4) — in the following steps:

   Step 1 — Application of the reimbursement rates to the eligible costs

   Step 2 — Limit to the maximum grant amount

   Step 3 — Reduction due to the no-profit rule

   Step 4 — Reduction due to substantial errors, irregularities or fraud or serious breach of obligations
5.3.1 Step 1 — Application of the reimbursement rates to the eligible costs

The reimbursement rate(s) (see Article 5.2) are applied to the eligible costs (actual costs, unit costs and flat-rate costs; see Article 6) declared by the beneficiaries and linked third parties (see Article 20) and approved by the Commission (see Article 21).

5.3.2 Step 2 — Limit to the maximum grant amount

If the amount obtained following Step 1 is higher than the maximum grant amount set out in Article 5.1, it will be limited to the latter.

5.3.3 Step 3 — Reduction due to the no-profit rule

The grant must not produce a profit.

‘Profit’ means the surplus of the amount obtained following Steps 1 and 2 plus the action’s total receipts, over the action’s total eligible costs.

The ‘action’s total eligible costs’ are the consolidated total eligible costs approved by the Commission.

The ‘action’s total receipts’ are the consolidated total receipts generated during its duration (see Article 3).

The following are considered receipts:

(a) income generated by the action; if the income is generated from selling equipment or other assets purchased under the Agreement, the receipt is up to the amount declared as eligible under the Agreement;

(b) financial contributions given by third parties to the beneficiary or to a linked third party specifically to be used for the action, and

(c) in-kind contributions provided by third parties free of charge and specifically to be used for the action, if they have been declared as eligible costs.

The following are however not considered receipts:

(a) income generated by exploiting the action’s results (see Article 28);

(b) financial contributions by third parties, if they may be used to cover costs other than the eligible costs (see Article 6);

(c) financial contributions by third parties with no obligation to repay any amount unused at the end of the period set out in Article 3.

If there is a profit, it will be deducted from the amount obtained following Steps 1 and 2.

5.3.4 Step 4 — Reduction due to substantial errors, irregularities or fraud or serious breach of obligations — Reduced grant amount — Calculation

If the grant is reduced (see Article 43), the Commission will calculate the reduced grant amount by deducting the amount of the reduction (calculated in proportion to the seriousness of the errors,
irregularities or fraud or breach of obligations, in accordance with Article 43.2) from the maximum grant amount set out in Article 5.1.

The final grant amount will be the lower of the following two:

- the amount obtained following Steps 1 to 3 or
- the reduced grant amount following Step 4.

5.4 Revised final grant amount — Calculation

If — after the payment of the balance (in particular, after checks, reviews, audits or investigations; see Article 22) — the Commission rejects costs (see Article 42) or reduces the grant (see Article 43), it will calculate the ‘revised final grant amount’ for the beneficiary concerned by the findings.

This amount is calculated by the Commission on the basis of the findings, as follows:

- in case of rejection of costs: by applying the reimbursement rate to the revised eligible costs approved by the Commission for the beneficiary concerned;
- in case of reduction of the grant: by calculating the concerned beneficiary’s share in the grant amount reduced in proportion to the seriousness of the errors, irregularities or fraud or breach of obligations (see Article 43.2).

In case of rejection of costs and reduction of the grant, the revised final grant amount for the beneficiary concerned will be the lower of the two amounts above.

ARTICLE 6 — ELIGIBLE AND INELIGIBLE COSTS

6.1 General conditions for costs to be eligible

‘Eligible costs’ are costs that meet the following criteria:

(a) for actual costs:

(i) they must be actually incurred by the beneficiary;

(ii) they must be incurred in the period set out in Article 3, with the exception of costs relating to the submission of the periodic report for the last reporting period and the final report (see Article 20);

(iii) they must be indicated in the estimated budget set out in Annex 2;

(iv) they must be incurred in connection with the action as described in Annex 1 and necessary for its implementation;

(v) they must be identifiable and verifiable, in particular recorded in the beneficiary’s accounts in accordance with the accounting standards applicable in the country where the beneficiary is established and with the beneficiary’s usual cost accounting practices;

(vi) they must comply with the applicable national law on taxes, labour and social security, and
(vii) they must be reasonable, justified and must comply with the principle of sound financial management, in particular regarding economy and efficiency;

(b) for unit costs:

(i) they must be calculated as follows:

{amounts per unit set out in Annex 2a or calculated by the beneficiary in accordance with its usual cost accounting practices (see Article 6.2, Point A and Article 6.2.D.5)

multiplied by

the number of actual units};

(ii) the number of actual units must comply with the following conditions:

- the units must be actually used or produced in the period set out in Article 3;
- the units must be necessary for implementing the action or produced by it, and
- the number of units must be identifiable and verifiable, in particular supported by records and documentation (see Article 18);

(c) for flat-rate costs:

(i) they must be calculated by applying the flat-rate set out in Annex 2, and

(ii) the costs (actual costs or unit costs) to which the flat-rate is applied must comply with the conditions for eligibility set out in this Article.

6.2 Specific conditions for costs to be eligible

Costs are eligible if they comply with the general conditions (see above) and the specific conditions set out below for each of the following budget categories:

A. direct personnel costs;
B. direct costs of subcontracting;
C. not applicable;
D. other direct costs;
E. indirect costs;
F. not applicable.

‘Direct costs’ are costs that are directly linked to the action implementation and can therefore be attributed to it directly. They must not include any indirect costs (see Point E below).

‘Indirect costs’ are costs that are not directly linked to the action implementation and therefore cannot be attributed directly to it.

A. Direct personnel costs

Types of eligible personnel costs
A.1 Personnel costs are eligible, if they are related to personnel working for the beneficiary under an employment contract (or equivalent appointing act) and assigned to the action (‘costs for employees (or equivalent)’). They must be limited to salaries (including during parental leave), social security contributions, taxes and other costs included in the remuneration, if they arise from national law or the employment contract (or equivalent appointing act).

Beneficiaries that are non-profit legal entities\(^1\) may also declare as personnel costs additional remuneration for personnel assigned to the action (including payments on the basis of supplementary contracts regardless of their nature), if:

(a) it is part of the beneficiary’s usual remuneration practices and is paid in a consistent manner whenever the same kind of work or expertise is required;

(b) the criteria used to calculate the supplementary payments are objective and generally applied by the beneficiary, regardless of the source of funding used.

‘Additional remuneration’ means any part of the remuneration which exceeds what the person would be paid for time worked in projects funded by national schemes.

Additional remuneration for personnel assigned to the action is eligible up to the following amount:

(a) if the person works full time and exclusively on the action during the full year: up to EUR 8 000;

(b) if the person works exclusively on the action but not full-time or not for the full year: up to the corresponding pro-rata amount of EUR 8 000, or

(c) if the person does not work exclusively on the action: up to a pro-rata amount calculated as follows:

\[
\text{EUR 8 000} \div \text{the number of annual productive hours (see below)} \times \text{the number of hours that the person has worked on the action during the year}.
\]

A.2 The costs for natural persons working under a direct contract with the beneficiary other than an employment contract are eligible personnel costs, if:

(a) the person works under conditions similar to those of an employee (in particular regarding the way the work is organised, the tasks that are performed and the premises where they are performed);

(b) the result of the work carried out belongs to the beneficiary (unless exceptionally agreed otherwise), and

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\(^1\) For the definition, see Article 2.1(14) of the Rules for Participation Regulation No 1290/2013: ‘non-profit legal entity’ means a legal entity which by its legal form is non-profit-making or which has a legal or statutory obligation not to distribute profits to its shareholders or individual members.
(c) the costs are not significantly different from those for personnel performing similar tasks under an employment contract with the beneficiary.

A.3 The **costs of personnel seconded by a third party against payment** are eligible personnel costs, if the conditions in Article 11.1 are met.

A.4 **Costs of owners** of beneficiaries that are small and medium-sized enterprises (‘SME owners’) who are working on the action and who do not receive a salary are eligible personnel costs, if they correspond to the amount per unit set out in Annex 2a multiplied by the number of actual hours worked on the action.

A.5 **Costs of ‘beneficiaries that are natural persons’** not receiving a salary are eligible personnel costs, if they correspond to the amount per unit set out in Annex 2a multiplied by the number of actual hours worked on the action.

**Calculation**

Personnel costs must be calculated by the beneficiaries as follows:

\[
\text{hourly rate} \times \text{number of actual hours worked on the action},
\]

plus

for non-profit legal entities: additional remuneration to personnel assigned to the action under the conditions set out above (Point A.1).

The number of actual hours declared for a person must be identifiable and verifiable (see Article 18).

The total number of hours declared in EU or Euratom grants, for a person for a year, cannot be higher than the annual productive hours used for the calculations of the hourly rate. Therefore, the maximum number of hours that can be declared for the grant are:

\[
\text{number of annual productive hours for the year (see below)} - \text{total number of hours declared by the beneficiary, for that person in that year, for other EU or Euratom grants}.
\]

The **hourly rate** is one of the following:

(a) for personnel costs declared as **actual costs** (i.e. budget categories A.1, A.2, A.3): the hourly rate is calculated *per full financial year*, as follows:

\[
\text{actual annual personnel costs (excluding additional remuneration) for the person} / \text{number of annual productive hours}.
\]

using the personnel costs and the number of productive hours for each full financial year covered by the reporting period concerned. If a financial year is not closed at the end of the
reporting period, the beneficiaries must use the hourly rate of the last closed financial year available.

For the ‘number of annual productive hours’, the beneficiaries may choose one of the following:

(i) ‘fixed number of hours’: 1,720 hours for persons working full time (or corresponding pro-rata for persons not working full time);

(ii) ‘individual annual productive hours’: the total number of hours worked by the person in the year for the beneficiary, calculated as follows:

   \{\text{annual workable hours of the person (according to the employment contract, applicable collective labour agreement or national law)}

   \text{plus}

   \text{overtime worked}

   \text{minus}

   \text{absences (such as sick leave and special leave)}\}.

‘Annual workable hours’ means the period during which the personnel must be working, at the employer’s disposal and carrying out his/her activity or duties under the employment contract, applicable collective labour agreement or national working time legislation.

If the contract (or applicable collective labour agreement or national working time legislation) does not allow to determine the annual workable hours, this option cannot be used;

(iii) ‘standard annual productive hours’: the ‘standard number of annual hours’ generally applied by the beneficiary for its personnel in accordance with its usual cost accounting practices. This number must be at least 90% of the ‘standard annual workable hours’.

If there is no applicable reference for the standard annual workable hours, this option cannot be used.

For all options, the actual time spent on parental leave by a person assigned to the action may be deducted from the number of annual productive hours.

As an alternative, beneficiaries may calculate the hourly rate per month, as follows:

\{\text{actual monthly personnel cost (excluding additional remuneration) for the person}

\text{divided by}

\{\text{number of annual productive hours / 12}\}\}

using the personnel costs for each month and (one twelfth of) the annual productive hours calculated according to either option (i) or (iii) above, i.e.:

- fixed number of hours or

- standard annual productive hours.
Time spent on **parental leave** may not be deducted when calculating the hourly rate per month. However, beneficiaries may declare personnel costs incurred in periods of parental leave in proportion to the time the person worked on the action in that financial year.

If parts of a basic remuneration are generated over a period longer than a month, the beneficiaries may include only the share which is generated in the month (irrespective of the amount actually paid for that month).

Each beneficiary must use only one option (per full financial year or per month) for each full financial year;

(b) for personnel costs declared on the basis of **unit costs** (i.e. budget categories A.1, A.2, A.4, A.5):
   the hourly rate is one of the following:

   (i) for SME owners or beneficiaries that are natural persons: the hourly rate set out in Annex 2a (see Points A.4 and A.5 above), or

   (ii) for personnel costs declared on the basis of the beneficiary’s usual cost accounting practices: the hourly rate calculated by the beneficiary in accordance with its usual cost accounting practices, if:

       - the cost accounting practices used are applied in a consistent manner, based on objective criteria, regardless of the source of funding;

       - the hourly rate is calculated using the actual personnel costs recorded in the beneficiary’s accounts, excluding any ineligible cost or costs included in other budget categories.

The actual personnel costs may be adjusted by the beneficiary on the basis of budgeted or estimated elements. Those elements must be relevant for calculating the personnel costs, reasonable and correspond to objective and verifiable information;

and

- the hourly rate is calculated using the number of annual productive hours (see above).

**B. Direct costs of subcontracting** (including related duties, taxes and charges such as non-deductible value added tax (VAT) paid by the beneficiary) are eligible if the conditions in Article 13.1.1 are met.

**C. Direct costs of providing financial support to third parties**

Not applicable

**D. Other direct costs**

D.1 **Travel costs and related subsistence allowances** (including related duties, taxes and charges such as non-deductible value added tax (VAT) paid by the beneficiary) are eligible if they are in line with the beneficiary’s usual practices on travel.

D.2 The **depreciation costs of equipment, infrastructure or other assets** (new or second-hand) as recorded in the beneficiary’s accounts are eligible, if they were purchased in accordance with
Article 10.1.1 and written off in accordance with international accounting standards and the beneficiary’s usual accounting practices.

The costs of renting or leasing equipment, infrastructure or other assets (including related duties, taxes and charges such as non-deductible value added tax (VAT) paid by the beneficiary) are also eligible, if they do not exceed the depreciation costs of similar equipment, infrastructure or assets and do not include any financing fees.

The costs of equipment, infrastructure or other assets contributed in-kind against payment are eligible, if they do not exceed the depreciation costs of similar equipment, infrastructure or assets, do not include any financing fees and if the conditions in Article 11.1 are met.

The only portion of the costs that will be taken into account is that which corresponds to the duration of the action and rate of actual use for the purposes of the action.

D.3 Costs of other goods and services (including related duties, taxes and charges such as non-deductible value added tax (VAT) paid by the beneficiary) are eligible, if they are:

(a) purchased specifically for the action and in accordance with Article 10.1.1 or

(b) contributed in kind against payment and in accordance with Article 11.1.

Such goods and services include, for instance, consumables and supplies, dissemination (including open access), protection of results, certificates on the financial statements (if they are required by the Agreement), certificates on the methodology, translations and publications.

D.4 Capitalised and operating costs of ‘large research infrastructure’\(^2\) directly used for the action are eligible, if:

(a) the value of the large research infrastructure represents at least 75% of the total fixed assets (at historical value in its last closed balance sheet before the date of the signature of the Agreement or as determined on the basis of the rental and leasing costs of the research infrastructure\(^3\));

(b) the beneficiary’s methodology for declaring the costs for large research infrastructure has been positively assessed by the Commission (‘\textit{ex-ante assessment}’);

(c) the beneficiary declares as direct eligible costs only the portion which corresponds to the duration of the action and the rate of actual use for the purposes of the action, and

(d) they comply with the conditions as further detailed in the annotations to the H2020 grant agreements.

\(^2\) ‘\textit{Large research infrastructure}’ means research infrastructure of a total value of at least EUR 20 million, for a beneficiary, calculated as the sum of historical asset values of each individual research infrastructure of that beneficiary, as they appear in its last closed balance sheet before the date of the signature of the Agreement or as determined on the basis of the rental and leasing costs of the research infrastructure.

\(^3\) For the definition, see Article 2(6) of the H2020 Framework Programme Regulation No 1291/2013: ‘\textit{Research infrastructure}’ are facilities, resources and services that are used by the research communities to conduct research and foster innovation in their fields. Where relevant, they may be used beyond research, e.g. for education or public services. They include: major scientific equipment (or sets of instruments); knowledge-based resources such as collections, archives or scientific data; e-infrastructures such as data and computing systems and communication networks; and any other infrastructure of a unique nature essential to achieve excellence in research and innovation. Such infrastructures may be ‘single-sited’, ‘virtual’ or ‘distributed’.
D.5 Costs of internally invoiced goods and services directly used for the action are eligible, if:

(a) they are declared on the basis of a unit cost calculated in accordance with the beneficiary’s usual cost accounting practices;

(b) the cost accounting practices used are applied in a consistent manner, based on objective criteria, regardless of the source of funding;

(c) the unit cost is calculated using the actual costs for the good or service recorded in the beneficiary’s accounts, excluding any ineligible cost or costs included in other budget categories.

The actual costs may be adjusted by the beneficiary on the basis of budgeted or estimated elements. Those elements must be relevant for calculating the costs, reasonable and correspond to objective and verifiable information;

(d) the unit cost excludes any costs of items which are not directly linked to the production of the invoiced goods or service.

‘Internally invoiced goods and services’ means goods or services which are provided by the beneficiary directly for the action and which the beneficiary values on the basis of its usual cost accounting practices.

E. Indirect costs

Indirect costs are eligible if they are declared on the basis of the flat-rate of 25% of the eligible direct costs (see Article 5.2 and Points A to D above), from which are excluded:

(a) costs of subcontracting and

(b) costs of in-kind contributions provided by third parties which are not used on the beneficiary’s premises;

(c) not applicable;

(d) not applicable.

Beneficiaries receiving an operating grant\(^4\) financed by the EU or Euratom budget cannot declare indirect costs for the period covered by the operating grant, unless they can demonstrate that the operating grant does not cover any costs of the action.

F. Specific cost category(ies)

Not applicable

6.3 Conditions for costs of linked third parties to be eligible

Costs incurred by linked third parties are eligible if they fulfil — mutatis mutandis — the general and specific conditions for eligibility set out in this Article (Article 6.1 and 6.2) and Article 14.1.1.

6.4 Conditions for in-kind contributions provided by third parties free of charge to be eligible

In-kind contributions provided free of charge are eligible direct costs (for the beneficiary or linked third party), if the costs incurred by the third party fulfil — mutatis mutandis — the general and specific conditions for eligibility set out in this Article (Article 6.1 and 6.2) and Article 12.1.

6.5 Ineligible costs

‘Ineligible costs’ are:

(a) costs that do not comply with the conditions set out above (Article 6.1 to 6.4), in particular:

   (i) costs related to return on capital;
   (ii) debt and debt service charges;
   (iii) provisions for future losses or debts;
   (iv) interest owed;
   (v) doubtful debts;
   (vi) currency exchange losses;
   (vii) bank costs charged by the beneficiary’s bank for transfers from the Commission;
   (viii) excessive or reckless expenditure;
   (ix) deductible VAT;
   (x) costs incurred during suspension of the implementation of the action (see Article 49);

(b) costs declared under another EU or Euratom grant (including grants awarded by a Member State and financed by the EU or Euratom budget and grants awarded by bodies other than the Commission for the purpose of implementing the EU or Euratom budget); in particular, indirect costs if the beneficiary is already receiving an operating grant financed by the EU or Euratom budget in the same period, unless it can demonstrate that the operating grant does not cover any costs of the action.

6.6 Consequences of declaration of ineligible costs

Declared costs that are ineligible will be rejected (see Article 42).

This may also lead to any of the other measures described in Chapter 6.

CHAPTER 4 RIGHTS AND OBLIGATIONS OF THE PARTIES
SECTION 1  RIGHTS AND OBLIGATIONS RELATED TO IMPLEMENTING THE ACTION

ARTICLE 7 — GENERAL OBLIGATION TO PROPERLY IMPLEMENT THE ACTION

7.1 General obligation to properly implement the action

The beneficiaries must implement the action as described in Annex 1 and in compliance with the provisions of the Agreement and all legal obligations under applicable EU, international and national law.

7.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 8 — RESOURCES TO IMPLEMENT THE ACTION — THIRD PARTIES INVOLVED IN THE ACTION

The beneficiaries must have the appropriate resources to implement the action.

If it is necessary to implement the action, the beneficiaries may:

- purchase goods, works and services (see Article 10);
- use in-kind contributions provided by third parties against payment (see Article 11);
- use in-kind contributions provided by third parties free of charge (see Article 12);
- call upon subcontractors to implement action tasks described in Annex 1 (see Article 13);
- call upon linked third parties to implement action tasks described in Annex 1 (see Article 14);
- call upon international partners to implement action tasks described in Annex 1 (see Article 14a).

In these cases, the beneficiaries retain sole responsibility towards the Commission and the other beneficiaries for implementing the action.

ARTICLE 9 — IMPLEMENTATION OF ACTION TASKS BY BENEFICIARIES NOT RECEIVING EU FUNDING

9.1 Rules for the implementation of action tasks by beneficiaries not receiving EU funding

Beneficiaries that are not eligible for EU funding (‘beneficiaries not receiving EU funding’) must implement the action tasks attributed to them in Annex 1 in accordance with Article 7.1.

Their costs are estimated in Annex 2 but:

- will not be reimbursed and
Chapter 3, Articles 10 to 15, 18.1.2, 20.3(b), 20.4(b), 20.6, 21, 23a, 26.4, 27.2, 28.1, 28.2, 30.3, 31.5, 40, 42, 43, 44, 47 and 48 do not apply to these beneficiaries.

They will not be subject to financial checks, reviews and audits under Article 22.

Beneficiaries not receiving EU funding may provide in-kind contributions to another beneficiary. In this case, they will be considered as a third party for the purpose of Articles 11 and 12.

9.2 Consequences of non-compliance

If a beneficiary not receiving EU funding breaches any of its obligations under this Article, its participation in the Agreement may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6 that are applicable to it.

ARTICLE 10 — PURCHASE OF GOODS, WORKS OR SERVICES

10.1 Rules for purchasing goods, works or services

10.1.1 If necessary to implement the action, the beneficiaries may purchase goods, works or services. The beneficiaries must make such purchases ensuring the best value for money or, if appropriate, the lowest price. In doing so, they must avoid any conflict of interests (see Article 35).

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards their contractors.

10.1.2 Beneficiaries that are ‘contracting authorities’ within the meaning of Directive 2004/18/EC\(^5\) (or 2014/24/EU\(^6\)) or ‘contracting entities’ within the meaning of Directive 2004/17/EC\(^7\) (or 2014/25/EU\(^8\)) must comply with the applicable national law on public procurement.

10.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under Article 10.1.1, the costs related to the contract concerned will be ineligible (see Article 6) and will be rejected (see Article 42).


If a beneficiary breaches any of its obligations under Article 10.1.2, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

**ARTICLE 11 — USE OF IN-KIND CONTRIBUTIONS PROVIDED BY THIRD PARTIES AGAINST PAYMENT**

11.1 Rules for the use of in-kind contributions against payment

If necessary to implement the action, the beneficiaries may use in-kind contributions provided by third parties against payment.

The beneficiaries may declare costs related to the payment of in-kind contributions as eligible (see Article 6.1 and 6.2), up to the third parties’ costs for the seconded persons, contributed equipment, infrastructure or other assets or other contributed goods and services.

The third parties and their contributions must be set out in Annex 1. The Commission may however approve in-kind contributions not set out in Annex 1 without amendment (see Article 55), if:

- they are specifically justified in the periodic technical report and
- their use does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards the third parties.

11.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the costs related to the payment of the in-kind contribution will be ineligible (see Article 6) and will be rejected (see Article 42).

Such breaches may also lead to any of the other measures described in Chapter 6.

**ARTICLE 12 — USE OF IN-KIND CONTRIBUTIONS PROVIDED BY THIRD PARTIES FREE OF CHARGE**

12.1 Rules for the use of in-kind contributions free of charge

If necessary to implement the action, the beneficiaries may use in-kind contributions provided by third parties free of charge.

The beneficiaries may declare costs incurred by the third parties for the seconded persons, contributed equipment, infrastructure or other assets or other contributed goods and services as eligible in accordance with Article 6.4.

The third parties and their contributions must be set out in Annex 1. The Commission may however approve in-kind contributions not set out in Annex 1 without amendment (see Article 55), if:

- they are specifically justified in the periodic technical report and
- their use does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards the third parties.

12.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the costs incurred by the third parties related to the in-kind contribution will be ineligible (see Article 6) and will be rejected (see Article 42).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 13 — IMPLEMENTATION OF ACTION TASKS BY SUBCONTRACTORS

13.1 Rules for subcontracting action tasks

13.1.1 If necessary to implement the action, the beneficiaries may award subcontracts covering the implementation of certain action tasks described in Annex 1.

Subcontracting may cover only a limited part of the action.

The beneficiaries must award the subcontracts ensuring the best value for money or, if appropriate, the lowest price. In doing so, they must avoid any conflict of interests (see Article 35).

The tasks to be implemented and the estimated cost for each subcontract must be set out in Annex 1 and the total estimated costs of subcontracting per beneficiary must be set out in Annex 2. The Commission may however approve subcontracts not set out in Annex 1 and 2 without amendment (see Article 55), if:

- they are specifically justified in the periodic technical report and
- they do not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards their subcontractors.

13.1.2 The beneficiaries must ensure that their obligations under Articles 35, 36, 38 and 46 also apply to the subcontractors.

Beneficiaries that are ‘contracting authorities’ within the meaning of Directive 2004/18/EC (or 2014/24/EU) or ‘contracting entities’ within the meaning of Directive 2004/17/EC (or 2014/25/EU) must comply with the applicable national law on public procurement.

13.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under Article 13.1.1, the costs related to the subcontract concerned will be ineligible (see Article 6) and will be rejected (see Article 42).
If a beneficiary breaches any of its obligations under Article 13.1.2, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

**ARTICLE 14 — IMPLEMENTATION OF ACTION TASKS BY LINKED THIRD PARTIES**

14.1 Rules for calling upon linked third parties to implement part of the action

14.1.1 The following affiliated entities\(^\text{10}\) and third parties with a legal link to a beneficiary\(^\text{11}\) (‘linked third parties’) may implement the action tasks attributed to them in Annex 1:

- UNIVERSITAIR ZIEKENHUIS ANTWERPEN (UZA), affiliated or linked to UANTWERPEN

The linked third parties may declare as eligible the costs they incur for implementing the action tasks in accordance with Article 6.3.

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards their linked third parties.

14.1.2 The beneficiaries must ensure that their obligations under Articles 18, 20, 35, 36 and 38 also apply to their linked third parties.

14.2 Consequences of non-compliance

If any obligation under Article 14.1.1 is breached, the costs of the linked third party will be ineligible (see Article 6) and will be rejected (see Article 42).

If any obligation under Article 14.1.2 is breached, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

**ARTICLE 14a — IMPLEMENTATION OF ACTION TASKS BY INTERNATIONAL PARTNERS**

\(^{10}\) For the definition see Article 2.1(2) Rules for Participation Regulation No 1290/2013: ‘affiliated entity’ means any legal entity that is:
- under the direct or indirect control of a participant, or
- under the same direct or indirect control as the participant, or
- directly or indirectly controlling a participant.

‘Control’ may take any of the following forms:

(a) the direct or indirect holding of more than 50% of the nominal value of the issued share capital in the legal entity concerned, or of a majority of the voting rights of the shareholders or associates of that entity;

(b) the direct or indirect holding, in fact or in law, of decision-making powers in the legal entity concerned.

However the following relationships between legal entities shall not in themselves be deemed to constitute controlling relationships:

(a) the same public investment corporation, institutional investor or venture-capital company has a direct or indirect holding of more than 50% of the nominal value of the issued share capital or a majority of voting rights of the shareholders or associates;

(b) the legal entities concerned are owned or supervised by the same public body.

\(^{11}\) ‘Third party with a legal link to a beneficiary’ is any legal entity which has a legal link to the beneficiary implying collaboration that is not limited to the action.
ARTICLE 15 — FINANCIAL SUPPORT TO THIRD PARTIES

15.1 Rules for providing financial support to third parties
Not applicable

15.2 Financial support in the form of prizes
Not applicable

15.3 Consequences of non-compliance
Not applicable

ARTICLE 16 — PROVISION OF TRANS-NATIONAL OR VIRTUAL ACCESS TO RESEARCH INFRASTRUCTURE

16.1 Rules for providing trans-national access to research infrastructure
Not applicable

16.2 Rules for providing virtual access to research infrastructure
Not applicable

16.3 Consequences of non-compliance
Not applicable

SECTION 2 RIGHTS AND OBLIGATIONS RELATED TO THE GRANT ADMINISTRATION

ARTICLE 17 — GENERAL OBLIGATION TO INFORM

17.1 General obligation to provide information upon request
The beneficiaries must provide — during implementation of the action or afterwards and in accordance with Article 41.2 — any information requested in order to verify eligibility of the costs, proper implementation of the action and compliance with any other obligation under the Agreement.

17.2 Obligation to keep information up to date and to inform about events and circumstances likely to affect the Agreement
Each beneficiary must keep information stored in the Participant Portal Beneficiary Register (via the electronic exchange system; see Article 52) up to date, in particular, its name, address, legal representatives, legal form and organisation type.
Each beneficiary must immediately inform the coordinator — which must immediately inform the Commission and the other beneficiaries — of any of the following:

(a) **events** which are likely to affect significantly or delay the implementation of the action or the EU's financial interests, in particular:

   (i) changes in its legal, financial, technical, organisational or ownership situation or those of its linked third parties and

   (ii) changes in the name, address, legal form, organisation type of its linked third parties;

(b) **circumstances** affecting:

   (i) the decision to award the grant or

   (ii) compliance with requirements under the Agreement.

### 17.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

**ARTICLE 18 — KEEPING RECORDS — SUPPORTING DOCUMENTATION**

#### 18.1 Obligation to keep records and other supporting documentation

The beneficiaries must — for a period of five years after the payment of the balance — keep records and other supporting documentation in order to prove the proper implementation of the action and the costs they declare as eligible.

They must make them available upon request (see Article 17) or in the context of checks, reviews, audits or investigations (see Article 22).

If there are on-going checks, reviews, audits, investigations, litigation or other pursuits of claims under the Agreement (including the extension of findings; see Article 22), the beneficiaries must keep the records and other supporting documentation until the end of these procedures.

The beneficiaries must keep the original documents. Digital and digitalised documents are considered originals if they are authorised by the applicable national law. The Commission may accept non-original documents if it considers that they offer a comparable level of assurance.

#### 18.1.1 Records and other supporting documentation on the scientific and technical implementation

The beneficiaries must keep records and other supporting documentation on scientific and technical implementation of the action in line with the accepted standards in the respective field.

#### 18.1.2 Records and other documentation to support the costs declared
The beneficiaries must keep the records and documentation supporting the costs declared, in particular the following:

(a) for **actual costs**: adequate records and other supporting documentation to prove the costs declared, such as contracts, subcontracts, invoices and accounting records. In addition, the beneficiaries' usual cost accounting practices and internal control procedures must enable direct reconciliation between the amounts declared, the amounts recorded in their accounts and the amounts stated in the supporting documentation;

(b) for **unit costs**: adequate records and other supporting documentation to prove the number of units declared. Beneficiaries do not need to identify the actual eligible costs covered or to keep or provide supporting documentation (such as accounting statements) to prove the amount per unit.

In addition, **for unit costs calculated in accordance with the beneficiary's usual cost accounting practices**, the beneficiaries must keep adequate records and documentation to prove that the cost accounting practices used comply with the conditions set out in Article 6.2.

The beneficiaries and linked third parties may submit to the Commission, for approval, a certificate (drawn up in accordance with Annex 6) stating that their usual cost accounting practices comply with these conditions (‘**certificate on the methodology**’). If the certificate is approved, costs declared in line with this methodology will not be challenged subsequently, unless the beneficiaries have concealed information for the purpose of the approval.

(c) for **flat-rate costs**: adequate records and other supporting documentation to prove the eligibility of the costs to which the flat-rate is applied. The beneficiaries do not need to identify the costs covered or provide supporting documentation (such as accounting statements) to prove the amount declared at a flat-rate.

In addition, **for personnel costs** (declared as actual costs or on the basis of unit costs), the beneficiaries must keep **time records** for the number of hours declared. The time records must be in writing and approved by the persons working on the action and their supervisors, at least monthly. In the absence of reliable time records of the hours worked on the action, the Commission may accept alternative evidence supporting the number of hours declared, if it considers that it offers an adequate level of assurance.

As an exception, for **persons working exclusively on the action**, there is no need to keep time records, if the beneficiary signs a **declaration** confirming that the persons concerned have worked exclusively on the action.

For costs declared by linked third parties (see Article 14), it is the beneficiary that must keep the originals of the financial statements and the certificates on the financial statements of the linked third parties.

**18.2 Consequences of non-compliance**

If a beneficiary breaches any of its obligations under this Article, costs insufficiently substantiated will be ineligible (see Article 6) and will be rejected (see Article 42), and the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.
ARTICLE 19 — SUBMISSION OF DELIVERABLES

19.1 Obligation to submit deliverables

The coordinator must submit the ‘deliverables’ identified in Annex 1, in accordance with the timing and conditions set out in it.

19.2 Consequences of non-compliance

If the coordinator breaches any of its obligations under this Article, the Commission may apply any of the measures described in Chapter 6.

ARTICLE 20 — REPORTING — PAYMENT REQUESTS

20.1 Obligation to submit reports

The coordinator must submit to the Commission (see Article 52) the technical and financial reports set out in this Article. These reports include requests for payment and must be drawn up using the forms and templates provided in the electronic exchange system (see Article 52).

20.2 Reporting periods

The action is divided into the following ‘reporting periods’:

- RP1: from month 1 to month 12
- RP2: from month 13 to month 24

20.3 Periodic reports — Requests for interim payments

The coordinator must submit a periodic report within 60 days following the end of each reporting period.

The periodic report must include the following:

(a) a ‘periodic technical report’ containing:

(i) an explanation of the work carried out by the beneficiaries;

(ii) an overview of the progress towards the objectives of the action, including milestones and deliverables identified in Annex 1.

This report must include explanations justifying the differences between work expected to be carried out in accordance with Annex 1 and that actually carried out.

The report must detail the exploitation and dissemination of the results and — if required in Annex 1 — an updated ‘plan for the exploitation and dissemination of the results’.

The report must indicate the communication activities;

(iii) a summary for publication by the Commission;

(iv) the answers to the ‘questionnaire’, covering issues related to the action implementation
and the economic and societal impact, notably in the context of the Horizon 2020 key performance indicators and the Horizon 2020 monitoring requirements;

(b) a ‘periodic financial report’ containing:

(i) an ‘individual financial statement’ (see Annex 4) from each beneficiary and from each linked third party, for the reporting period concerned.

   The individual financial statement must detail the eligible costs (actual costs, unit costs and flat-rate costs; see Article 6) for each budget category (see Annex 2).

   The beneficiaries and linked third parties must declare all eligible costs, even if — for actual costs, unit costs and flat-rate costs — they exceed the amounts indicated in the estimated budget (see Annex 2). Amounts which are not declared in the individual financial statement will not be taken into account by the Commission.

   If an individual financial statement is not submitted for a reporting period, it may be included in the periodic financial report for the next reporting period.

   The individual financial statements of the last reporting period must also detail the receipts of the action (see Article 5.3.3).

   Each beneficiary and each linked third party must certify that:

   - the information provided is full, reliable and true;
   - the costs declared are eligible (see Article 6);
   - the costs can be substantiated by adequate records and supporting documentation (see Article 18) that will be produced upon request (see Article 17) or in the context of checks, reviews, audits and investigations (see Article 22), and
   - for the last reporting period: that all the receipts have been declared (see Article 5.3.3);

(ii) an explanation of the use of resources and the information on subcontracting (see Article 13) and in-kind contributions provided by third parties (see Articles 11 and 12) from each beneficiary and from each linked third party, for the reporting period concerned;

(iii) not applicable;

(iv) a ‘periodic summary financial statement’, created automatically by the electronic exchange system, consolidating the individual financial statements for the reporting period concerned and including — except for the last reporting period — the request for interim payment.

20.4 Final report — Request for payment of the balance

In addition to the periodic report for the last reporting period, the coordinator must submit the final report within 60 days following the end of the last reporting period.

The final report must include the following:
(a) a ‘final technical report’ with a summary for publication containing:

(i) an overview of the results and their exploitation and dissemination;

(ii) the conclusions on the action, and

(iii) the socio-economic impact of the action;

(b) a ‘final financial report’ containing:

(i) a ‘final summary financial statement’, created automatically by the electronic exchange system, consolidating the individual financial statements for all reporting periods and including the request for payment of the balance and

(ii) a ‘certificate on the financial statements’ (drawn up in accordance with Annex 5) for each beneficiary and for each linked third party, if it requests a total contribution of EUR 325,000 or more, as reimbursement of actual costs and unit costs calculated on the basis of its usual cost accounting practices (see Article 5.2 and Article 6.2).

20.5 Information on cumulative expenditure incurred

Not applicable

20.6 Currency for financial statements and conversion into euro

Financial statements must be drafted in euro.

Beneficiaries and linked third parties with accounting established in a currency other than the euro must convert the costs recorded in their accounts into euro, at the average of the daily exchange rates published in the C series of the Official Journal of the European Union, calculated over the corresponding reporting period.

If no daily euro exchange rate is published in the Official Journal of the European Union for the currency in question, they must be converted at the average of the monthly accounting rates published on the Commission’s website, calculated over the corresponding reporting period.

Beneficiaries and linked third parties with accounting established in euro must convert costs incurred in another currency into euro according to their usual accounting practices.

20.7 Language of reports

All reports (technical and financial reports, including financial statements) must be submitted in the language of the Agreement.

20.8 Consequences of non-compliance

If the reports submitted do not comply with this Article, the Commission may suspend the payment deadline (see Article 47) and apply any of the other measures described in Chapter 6.

If the coordinator breaches its obligation to submit the reports and if it fails to comply with this obligation within 30 days following a written reminder, the Commission may terminate the Agreement (see Article 50) or apply any of the other measures described in Chapter 6.
ARTICLE 21 — PAYMENTS AND PAYMENT ARRANGEMENTS

21.1 Payments to be made

The following payments will be made to the coordinator:

- one pre-financing payment;
- one or more interim payments, on the basis of the request(s) for interim payment (see Article 20), and
- one payment of the balance, on the basis of the request for payment of the balance (see Article 20).

21.2 Pre-financing payment — Amount — Amount retained for the Guarantee Fund

The aim of the pre-financing is to provide the beneficiaries with a float. It remains the property of the EU until the payment of the balance.

The amount of the pre-financing payment will be EUR 3,996,656.00 (three million nine hundred and ninety six thousand six hundred and fifty six EURO).

The Commission will — except if Article 48 applies — make the pre-financing payment to the coordinator within 30 days, either from the entry into force of the Agreement (see Article 58) or from 10 days before the starting date of the action (see Article 3), whichever is the latest.

An amount of EUR 249,791.00 (two hundred and forty nine thousand seven hundred and ninety one EURO), corresponding to 5% of the maximum grant amount (see Article 5.1), is retained by the Commission from the pre-financing payment and transferred into the ‘Guarantee Fund’.

21.3 Interim payments — Amount — Calculation

Interim payments reimburse the eligible costs incurred for the implementation of the action during the corresponding reporting periods.

The Commission will pay to the coordinator the amount due as interim payment within 90 days from receiving the periodic report (see Article 20.3), except if Articles 47 or 48 apply.

Payment is subject to the approval of the periodic report. Its approval does not imply recognition of the compliance, authenticity, completeness or correctness of its content.

The amount due as interim payment is calculated by the Commission in the following steps:

Step 1 — Application of the reimbursement rates

Step 2 — Limit to 90% of the maximum grant amount

21.3.1 Step 1 — Application of the reimbursement rates

The reimbursement rate(s) (see Article 5.2) are applied to the eligible costs (actual costs, unit costs and flat-rate costs; see Article 6) declared by the beneficiaries and the linked third parties (see Article 20) and approved by the Commission (see above) for the concerned reporting period.
21.3.2 Step 2 — Limit to 90% of the maximum grant amount

The total amount of pre-financing and interim payments must not exceed 90% of the maximum grant amount set out in Article 5.1. The maximum amount for the interim payment will be calculated as follows:

\{
90\% \text{ of the maximum grant amount (see Article 5.1)} \\
\text{minus} \\
\text{pre-financing and previous interim payments}\}

21.4 Payment of the balance — Amount — Calculation — Release of the amount retained for the Guarantee Fund

The payment of the balance reimburses the remaining part of the eligible costs incurred by the beneficiaries for the implementation of the action.

If the total amount of earlier payments is greater than the final grant amount (see Article 5.3), the payment of the balance takes the form of a recovery (see Article 44).

If the total amount of earlier payments is lower than the final grant amount, the Commission will pay the balance within 90 days from receiving the final report (see Article 20.4), except if Articles 47 or 48 apply.

Payment is subject to the approval of the final report. Its approval does not imply recognition of the compliance, authenticity, completeness or correctness of its content.

The amount due as the balance is calculated by the Commission by deducting the total amount of pre-financing and interim payments (if any) already made, from the final grant amount determined in accordance with Article 5.3:

\{
\text{final grant amount (see Article 5.3)} \\
\text{minus} \\
\text{pre-financing and interim payments (if any made)}\}

At the payment of the balance, the amount retained for the Guarantee Fund (see above) will be released and:

- if the balance is positive: the amount released will be paid in full to the coordinator together with the amount due as the balance;
- if the balance is negative (payment of the balance taking the form of recovery): it will be deducted from the amount released (see Article 44.1.2). If the resulting amount:
  - is positive, it will be paid to the coordinator
  - is negative, it will be recovered.

The amount to be paid may however be offset — without the beneficiaries' consent — against any other amount owed by a beneficiary to the Commission or an executive agency (under the EU or
Euratom budget), up to the maximum EU contribution indicated, for that beneficiary, in the estimated budget (see Annex 2).

21.5 Notification of amounts due

When making payments, the Commission will formally notify to the coordinator the amount due, specifying whether it concerns an interim payment or the payment of the balance.

For the payment of the balance, the notification will also specify the final grant amount.

In the case of reduction of the grant or recovery of undue amounts, the notification will be preceded by the contradictory procedure set out in Articles 43 and 44.

21.6 Currency for payments

The Commission will make all payments in euro.

21.7 Payments to the coordinator — Distribution to the beneficiaries

Payments will be made to the coordinator.

Payments to the coordinator will discharge the Commission from its payment obligation.

The coordinator must distribute the payments between the beneficiaries without unjustified delay.

Pre-financing may however be distributed only:

(a) if the minimum number of beneficiaries set out in the call for proposals has acceded to the Agreement (see Article 56) and

(b) to beneficiaries that have acceded to the Agreement (see Article 56).

21.8 Bank account for payments

All payments will be made to the following bank account:

Name of bank: KBC BANK NV
Full name of the account holder: UNIVERSITEIT ANTWERPEN
IBAN code: BE90735007997232

21.9 Costs of payment transfers

The cost of the payment transfers is borne as follows:

- the Commission bears the cost of transfers charged by its bank;
- the beneficiary bears the cost of transfers charged by its bank;
- the party causing a repetition of a transfer bears all costs of the repeated transfer.

21.10 Date of payment
Payments by the Commission are considered to have been carried out on the date when they are debited to its account.

21.11 Consequences of non-compliance

21.11.1 If the Commission does not pay within the payment deadlines (see above), the beneficiaries are entitled to late-payment interest at the rate applied by the European Central Bank (ECB) for its main refinancing operations in euros (‘reference rate’), plus three and a half points. The reference rate is the rate in force on the first day of the month in which the payment deadline expires, as published in the C series of the Official Journal of the European Union.

If the late-payment interest is lower than or equal to EUR 200, it will be paid to the coordinator only upon request submitted within two months of receiving the late payment.

Late-payment interest is not due if all beneficiaries are EU Member States (including regional and local government authorities or other public bodies acting on behalf of a Member State for the purpose of this Agreement).

Suspension of the payment deadline or payments (see Articles 47 and 48) will not be considered as late payment.

Late-payment interest covers the period running from the day following the due date for payment (see above), up to and including the date of payment.

Late-payment interest is not considered for the purposes of calculating the final grant amount.

21.11.2 If the coordinator breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or the participation of the coordinator may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 22 — CHECKS, REVIEWS, AUDITS AND INVESTIGATIONS — EXTENSION OF FINDINGS

22.1 Checks, reviews and audits by the Commission

22.1.1 Right to carry out checks

The Commission will — during the implementation of the action or afterwards — check the proper implementation of the action and compliance with the obligations under the Agreement, including assessing deliverables and reports.

For this purpose the Commission may be assisted by external persons or bodies.

The Commission may also request additional information in accordance with Article 17. The Commission may request beneficiaries to provide such information to it directly.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

22.1.2 Right to carry out reviews
The Commission may — during the implementation of the action or afterwards — carry out reviews on the proper implementation of the action (including assessment of deliverables and reports), compliance with the obligations under the Agreement and continued scientific or technological relevance of the action.

Reviews may be started up to two years after the payment of the balance. They will be formally notified to the coordinator or beneficiary concerned and will be considered to have started on the date of the formal notification.

If the review is carried out on a third party (see Articles 10 to 16), the beneficiary concerned must inform the third party.

The Commission may carry out reviews directly (using its own staff) or indirectly (using external persons or bodies appointed to do so). It will inform the coordinator or beneficiary concerned of the identity of the external persons or bodies. They have the right to object to the appointment on grounds of commercial confidentiality.

The coordinator or beneficiary concerned must provide — within the deadline requested — any information and data in addition to deliverables and reports already submitted (including information on the use of resources). The Commission may request beneficiaries to provide such information to it directly.

The coordinator or beneficiary concerned may be requested to participate in meetings, including with external experts.

For on-the-spot reviews, the beneficiaries must allow access to their sites and premises, including to external persons or bodies, and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the review findings, a ‘review report’ will be drawn up.

The Commission will formally notify the review report to the coordinator or beneficiary concerned, which has 30 days to formally notify observations (‘contradictory review procedure’).

Reviews (including review reports) are in the language of the Agreement.

22.1.3 Right to carry out audits

The Commission may — during the implementation of the action or afterwards — carry out audits on the proper implementation of the action and compliance with the obligations under the Agreement.

Audits may be started up to two years after the payment of the balance. They will be formally notified to the coordinator or beneficiary concerned and will be considered to have started on the date of the formal notification.

If the audit is carried out on a third party (see Articles 10 to 16), the beneficiary concerned must inform the third party.

The Commission may carry out audits directly (using its own staff) or indirectly (using external persons or bodies appointed to do so). It will inform the coordinator or beneficiary concerned of the
identity of the external persons or bodies. They have the right to object to the appointment on grounds of commercial confidentiality.

The coordinator or beneficiary concerned must provide — within the deadline requested — any information (including complete accounts, individual salary statements or other personal data) to verify compliance with the Agreement. The Commission may request beneficiaries to provide such information to it directly.

For **on-the-spot** audits, the beneficiaries must allow access to their sites and premises, including to external persons or bodies, and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the audit findings, a ‘**draft audit report**’ will be drawn up.

The Commission will formally notify the draft audit report to the coordinator or beneficiary concerned, which has 30 days to formally notify observations (**‘contradictory audit procedure’**). This period may be extended by the Commission in justified cases.

The ‘**final audit report**’ will take into account observations by the coordinator or beneficiary concerned. The report will be formally notified to it.

Audits (including audit reports) are in the language of the Agreement.

The Commission may also access the beneficiaries’ statutory records for the periodical assessment of unit costs or flat-rate amounts.

**22.2 Investigations by the European Anti-Fraud Office (OLAF)**

Under Regulations No 883/2013\(^{16}\) and No 2185/96\(^{17}\) (and in accordance with their provisions and procedures), the European Anti-Fraud Office (OLAF) may — at any moment during implementation of the action or afterwards — carry out investigations, including on-the-spot checks and inspections, to establish whether there has been fraud, corruption or any other illegal activity affecting the financial interests of the EU.

**22.3 Checks and audits by the European Court of Auditors (ECA)**

Under Article 287 of the Treaty on the Functioning of the European Union (TFEU) and Article 161 of the Financial Regulation No 966/2012\(^{18}\), the European Court of Auditors (ECA) may — at any moment during implementation of the action or afterwards — carry out audits.

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\(^{17}\) Council Regulation (Euratom, EC) No 2185/1996 of 11 November 1996 concerning on-the-spot checks and inspections carried out by the Commission in order to protect the European Communities' financial interests against fraud and other irregularities (OJ L 292, 15.11.1996, p. 2).

The ECA has the right of access for the purpose of checks and audits.

**22.4 Checks, reviews, audits and investigations for international organisations**

Not applicable

**22.5 Consequences of findings in checks, reviews, audits and investigations — Extension of findings**

**22.5.1 Findings in this grant**

Findings in checks, reviews, audits or investigations carried out in the context of this grant may lead to the rejection of ineligible costs (see Article 42), reduction of the grant (see Article 43), recovery of undue amounts (see Article 44) or to any of the other measures described in Chapter 6.

Rejection of costs or reduction of the grant after the payment of the balance will lead to a revised final grant amount (see Article 5.4).

Findings in checks, reviews, audits or investigations may lead to a request for amendment for the modification of Annex 1 (see Article 55).

Checks, reviews, audits or investigations that find systemic or recurrent errors, irregularities, fraud or breach of obligations may also lead to consequences in other EU or Euratom grants awarded under similar conditions ('extension of findings from this grant to other grants').

Moreover, findings arising from an OLAF investigation may lead to criminal prosecution under national law.

**22.5.2 Findings in other grants**

The Commission may extend findings from other grants to this grant ('extension of findings from other grants to this grant'), if:

(a) the beneficiary concerned is found, in other EU or Euratom grants awarded under similar conditions, to have committed systemic or recurrent errors, irregularities, fraud or breach of obligations that have a material impact on this grant and

(b) those findings are formally notified to the beneficiary concerned — together with the list of grants affected by the findings — no later than two years after the payment of the balance of this grant.

The extension of findings may lead to the rejection of costs (see Article 42), reduction of the grant (see Article 43), recovery of undue amounts (see Article 44), suspension of payments (see Article 48), suspension of the action implementation (see Article 49) or termination (see Article 50).

**22.5.3 Procedure**

The Commission will formally notify the beneficiary concerned the systemic or recurrent errors and its intention to extend these audit findings, together with the list of grants affected.

22.5.3.1 If the findings concern eligibility of costs: the formal notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings;
(b) the request to submit revised financial statements for all grants affected;

(c) the correction rate for extrapolation established by the Commission on the basis of the systemic or recurrent errors, to calculate the amounts to be rejected if the beneficiary concerned:

(i) considers that the submission of revised financial statements is not possible or practicable or

(ii) does not submit revised financial statements.

The beneficiary concerned has 90 days from receiving notification to submit observations, revised financial statements or to propose a duly substantiated alternative correction method. This period may be extended by the Commission in justified cases.

The Commission may then start a rejection procedure in accordance with Article 42, on the basis of:

- the revised financial statements, if approved;
- the proposed alternative correction method, if accepted

or

- the initially notified correction rate for extrapolation, if it does not receive any observations or revised financial statements, does not accept the observations or the proposed alternative correction method or does not approve the revised financial statements.

22.5.3.2 If the findings concern substantial errors, irregularities or fraud or serious breach of obligations: the formal notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings and

(b) the flat-rate the Commission intends to apply according to the principle of proportionality.

The beneficiary concerned has 90 days from receiving notification to submit observations or to propose a duly substantiated alternative flat-rate.

The Commission may then start a reduction procedure in accordance with Article 43, on the basis of:

- the proposed alternative flat-rate, if accepted

or

- the initially notified flat-rate, if it does not receive any observations or does not accept the observations or the proposed alternative flat-rate.

22.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, any insufficiently substantiated costs will be ineligible (see Article 6) and will be rejected (see Article 42).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 23 — EVALUATION OF THE IMPACT OF THE ACTION
23.1 Right to evaluate the impact of the action

The Commission may carry out interim and final evaluations of the impact of the action measured against the objective of the EU programme.

Evaluations may be started during implementation of the action and up to five years after the payment of the balance. The evaluation is considered to start on the date of the formal notification to the coordinator or beneficiaries.

The Commission may make these evaluations directly (using its own staff) or indirectly (using external bodies or persons it has authorised to do so).

The coordinator or beneficiaries must provide any information relevant to evaluate the impact of the action, including information in electronic format.

23.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the Commission may apply the measures described in Chapter 6.

SECTION 3 RIGHTS AND OBLIGATIONS RELATED TO BACKGROUND AND RESULTS

SUBSECTION 1 GENERAL

ARTICLE 23a — MANAGEMENT OF INTELLECTUAL PROPERTY

23a.1 Obligation to take measures to implement the Commission Recommendation on the management of intellectual property in knowledge transfer activities

Beneficiaries that are universities or other public research organisations must take measures to implement the principles set out in Points 1 and 2 of the Code of Practice annexed to the Commission Recommendation on the management of intellectual property in knowledge transfer activities\(^{19}\).

This does not change the obligations set out in Subsections 2 and 3 of this Section.

The beneficiaries must ensure that researchers and third parties involved in the action are aware of them.

23a.2 Consequences of non-compliance

If a beneficiary breaches its obligations under this Article, the Commission may apply any of the measures described in Chapter 6.

SUBSECTION 2 RIGHTS AND OBLIGATIONS RELATED TO BACKGROUND

\(^{19}\) Commission Recommendation C(2008) 1329 of 10.4.2008 on the management of intellectual property in knowledge transfer activities and the Code of Practice for universities and other public research institutions attached to this recommendation.
ARTICLE 24 — AGREEMENT ON BACKGROUND

24.1 Agreement on background

The beneficiaries must identify and agree (in writing) on the background for the action (‘agreement on background’).

‘Background’ means any data, know-how or information — whatever its form or nature (tangible or intangible), including any rights such as intellectual property rights — that:

(a) is held by the beneficiaries before they acceded to the Agreement, and

(b) is needed to implement the action or exploit the results.

24.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 25 — ACCESS RIGHTS TO BACKGROUND

25.1 Exercise of access rights — Waiving of access rights — No sub-licensing

To exercise access rights, this must first be requested in writing (‘request for access’).

‘Access rights’ means rights to use results or background under the terms and conditions laid down in this Agreement.

Waivers of access rights are not valid unless in writing.

Unless agreed otherwise, access rights do not include the right to sub-license.

25.2 Access rights for other beneficiaries, for implementing their own tasks under the action

The beneficiaries must give each other access — on a royalty-free basis — to background needed to implement their own tasks under the action, unless the beneficiary that holds the background has — before acceding to the Agreement —:

(a) informed the other beneficiaries that access to its background is subject to legal restrictions or limits, including those imposed by the rights of third parties (including personnel), or

(b) agreed with the other beneficiaries that access would not be on a royalty-free basis.

25.3 Access rights for other beneficiaries, for exploiting their own results

The beneficiaries must give each other access — under fair and reasonable conditions — to background needed for exploiting their own results, unless the beneficiary that holds the background has — before acceding to the Agreement — informed the other beneficiaries that access to its background is subject to legal restrictions or limits, including those imposed by the rights of third parties (including personnel).
‘Fair and reasonable conditions’ means appropriate conditions, including possible financial terms or royalty-free conditions, taking into account the specific circumstances of the request for access, for example the actual or potential value of the results or background to which access is requested and/or the scope, duration or other characteristics of the exploitation envisaged.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

25.4 Access rights for affiliated entities

Unless otherwise agreed in the consortium agreement, access to background must also be given — under fair and reasonable conditions (see above; Article 25.3) and unless it is subject to legal restrictions or limits, including those imposed by the rights of third parties (including personnel) — to affiliated entities\(^{20}\) established in an EU Member State or ‘associated country’\(^{21}\), if this is needed to exploit the results generated by the beneficiaries to which they are affiliated.

Unless agreed otherwise (see above; Article 25.1), the affiliated entity concerned must make the request directly to the beneficiary that holds the background.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

25.5 Access rights for third parties

Not applicable

25.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

SUBSECTION 3 RIGHTS AND OBLIGATIONS RELATED TO RESULTS

ARTICLE 26 — OWNERSHIP OF RESULTS

26.1 Ownership by the beneficiary that generates the results

Results are owned by the beneficiary that generates them.

‘Results’ means any (tangible or intangible) output of the action such as data, knowledge or information — whatever its form or nature, whether it can be protected or not — that is generated in the action, as well as any rights attached to it, including intellectual property rights.

\(^{20}\) For the definition, see ‘affiliated entity’ footnote (Article 14.1).

\(^{21}\) For the definition, see Article 2.1(3) of the Rules for Participation Regulation No 1290/2013: ‘associated country’ means a third country which is party to an international agreement with the Union, as identified in Article 7 of Horizon 2020 Framework Programme Regulation No 1291/2013. Article 7 sets out the conditions for association of non-EU countries to Horizon 2020.
26.2 Joint ownership by several beneficiaries

Two or more beneficiaries own results jointly if:

(a) they have jointly generated them and

(b) it is not possible to:

(i) establish the respective contribution of each beneficiary, or

(ii) separate them for the purpose of applying for, obtaining or maintaining their protection (see Article 27).

The joint owners must agree (in writing) on the allocation and terms of exercise of their joint ownership (‘joint ownership agreement’), to ensure compliance with their obligations under this Agreement.

Unless otherwise agreed in the joint ownership agreement, each joint owner may grant non-exclusive licences to third parties to exploit jointly-owned results (without any right to sub-license), if the other joint owners are given:

(a) at least 45 days advance notice and

(b) fair and reasonable compensation.

Once the results have been generated, joint owners may agree (in writing) to apply another regime than joint ownership (such as, for instance, transfer to a single owner (see Article 30) with access rights for the others).

26.3 Rights of third parties (including personnel)

If third parties (including personnel) may claim rights to the results, the beneficiary concerned must ensure that it complies with its obligations under the Agreement.

If a third party generates results, the beneficiary concerned must obtain all necessary rights (transfer, licences or other) from the third party, in order to be able to respect its obligations as if those results were generated by the beneficiary itself.

If obtaining the rights is impossible, the beneficiary must refrain from using the third party to generate the results.

26.4 EU ownership, to protect results

26.4.1 The EU may — with the consent of the beneficiary concerned — assume ownership of results to protect them, if a beneficiary intends — up to four years after the period set out in Article 3 — to disseminate its results without protecting them, except in any of the following cases:

(a) the lack of protection is because protecting the results is not possible, reasonable or justified (given the circumstances); and

(b) the lack of protection is because there is a lack of potential for commercial or industrial exploitation, or
(c) the beneficiary intends to transfer the results to another beneficiary or third party established in an EU Member State or associated country, which will protect them.

Before the results are disseminated and unless any of the cases above under Points (a), (b) or (c) applies, the beneficiary must formally notify the Commission and at the same time inform it of any reasons for refusing consent. The beneficiary may refuse consent only if it can show that its legitimate interests would suffer significant harm.

If the Commission decides to assume ownership, it will formally notify the beneficiary concerned within 45 days of receiving notification.

No dissemination relating to these results may take place before the end of this period or, if the Commission takes a positive decision, until it has taken the necessary steps to protect the results.

26.4.2 The EU may — with the consent of the beneficiary concerned — assume ownership of results to protect them, if a beneficiary intends — up to four years after the period set out in Article 3 — to stop protecting them or not to seek an extension of protection, except in any of the following cases:

(a) the protection is stopped because of a lack of potential for commercial or industrial exploitation;

(b) an extension would not be justified given the circumstances.

A beneficiary that intends to stop protecting results or not seek an extension must — unless any of the cases above under Points (a) or (b) applies — formally notify the Commission at least 60 days before the protection lapses or its extension is no longer possible and at the same time inform it of any reasons for refusing consent. The beneficiary may refuse consent only if it can show that its legitimate interests would suffer significant harm.

If the Commission decides to assume ownership, it will formally notify the beneficiary concerned within 45 days of receiving notification.

26.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 27 — PROTECTION OF RESULTS — VISIBILITY OF EU FUNDING

27.1 Obligation to protect the results

Each beneficiary must examine the possibility of protecting its results and must adequately protect them — for an appropriate period and with appropriate territorial coverage — if:

(a) the results can reasonably be expected to be commercially or industrially exploited and

(b) protecting them is possible, reasonable and justified (given the circumstances).

When deciding on protection, the beneficiary must consider its own legitimate interests and the legitimate interests (especially commercial) of the other beneficiaries.
27.2 **EU ownership, to protect the results**

If a beneficiary intends not to protect its results, to stop protecting them or not seek an extension of protection, the EU may — under certain conditions (see Article 26.4) — assume ownership to ensure their (continued) protection.

27.3 **Information on EU funding**

Applications for protection of results (including patent applications) filed by or on behalf of a beneficiary must — unless the Commission requests or agrees otherwise or unless it is impossible — include the following:

“The project leading to this application has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 101003589”.

27.4 **Consequences of non-compliance**

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

**ARTICLE 28 — EXPLOITATION OF RESULTS**

28.1 **Obligation to exploit the results**

Each beneficiary must — up to four years after the period set out in Article 3 — take measures aiming to ensure ‘exploitation’ of its results (either directly or indirectly, in particular through transfer or licensing; see Article 30) by:

(a) using them in further research activities (outside the action);

(b) developing, creating or marketing a product or process;

(c) creating and providing a service, or

(d) using them in standardisation activities.

This does not change the security obligations in Article 37, which still apply.

28.2 **Results that could contribute to European or international standards — Information on EU funding**

If results are incorporated in a standard, the beneficiary concerned must — unless the Commission requests or agrees otherwise or unless it is impossible — ask the standardisation body to include the following statement in (information related to) the standard:

“Results incorporated in this standard received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 101003589”.

28.3 **Consequences of non-compliance**
If a beneficiary breaches any of its obligations under this Article, the grant may be reduced in accordance with Article 43.

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 29 — DISSEMINATION OF RESULTS — OPEN ACCESS — VISIBILITY OF EU FUNDING

29.1 Obligation to disseminate results

Unless it goes against their legitimate interests, each beneficiary must — as soon as possible — ‘disseminate’ its results by disclosing them to the public by appropriate means (other than those resulting from protecting or exploiting the results), including in scientific publications (in any medium).

This does not change the obligation to protect results in Article 27, the confidentiality obligations in Article 36, the security obligations in Article 37 or the obligations to protect personal data in Article 39, all of which still apply.

A beneficiary that intends to disseminate its results must give advance notice to the other beneficiaries of — unless agreed otherwise — at least 45 days, together with sufficient information on the results it will disseminate.

Any other beneficiary may object within — unless agreed otherwise — 30 days of receiving notification, if it can show that its legitimate interests in relation to the results or background would be significantly harmed. In such cases, the dissemination may not take place unless appropriate steps are taken to safeguard these legitimate interests.

If a beneficiary intends not to protect its results, it may — under certain conditions (see Article 26.4.1) — need to formally notify the Commission before dissemination takes place.

29.2 Open access to scientific publications

Each beneficiary must ensure open access (free of charge online access for any user) to all peer-reviewed scientific publications relating to its results.

In particular, it must:

(a) as soon as possible and at the latest on publication, deposit a machine-readable electronic copy of the published version or final peer-reviewed manuscript accepted for publication in a repository for scientific publications;

Moreover, the beneficiary must aim to deposit at the same time the research data needed to validate the results presented in the deposited scientific publications.

(b) ensure open access to the deposited publication — via the repository — at the latest:

(i) on publication, if an electronic version is available for free via the publisher, or

(ii) within six months of publication (twelve months for publications in the social sciences and humanities) in any other case.
(c) ensure open access — via the repository — to the bibliographic metadata that identify the 
deposited publication.

The bibliographic metadata must be in a standard format and must include all of the following:
- the terms “European Union (EU)” and “Horizon 2020”;
- the name of the action, acronym and grant number;
- the publication date, and length of embargo period if applicable, and
- a persistent identifier.

29.3 Open access to research data

The beneficiaries must deposit the digital research data generated in the action in a research data 
repository and take measures to make it possible for third parties to access, mine, exploit, reproduce 
and disseminate the data free of charge for any user, at the latest within 30 days after it has been 
generated.

This does not change the obligation to protect results in Article 27, the confidentiality obligations in 
Article 36, the security obligations in Article 37 or the obligations to protect personal data in Article 39, 
all of which still apply.

As an exception, the beneficiaries do not have to ensure open access, if the Commission agrees to 
replace the open access obligation by special access rights for third parties that need the research data 
to address the public health emergency. These access rights must include the right to access, mine, 
exploit and reproduce the data free of charge.

29.4 Information on EU funding — Obligation and right to use the EU emblem

Unless the Commission requests or agrees otherwise or unless it is impossible, any dissemination of 
results (in any form, including electronic) must:

(a) display the EU emblem and

(b) include the following text:

“This project has received funding from the European Union’s Horizon 2020 research and innovation 
programme under grant agreement No 101003589”.

When displayed together with another logo, the EU emblem must have appropriate prominence.

For the purposes of their obligations under this Article, the beneficiaries may use the EU emblem 
without first obtaining approval from the Commission.

This does not however give them the right to exclusive use.

Moreover, they may not appropriate the EU emblem or any similar trademark or logo, either by 
registration or by any other means.

29.5 Disclaimer excluding Commission responsibility
Any dissemination of results must indicate that it reflects only the author's view and that the Commission is not responsible for any use that may be made of the information it contains.

29.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 30 — TRANSFER AND LICENSING OF RESULTS

30.1 Transfer of ownership

Each beneficiary may transfer ownership of its results.

It must however ensure that its obligations under Articles 26.2, 26.4, 27, 28, 29, 30 and 31 also apply to the new owner and that this owner has the obligation to pass them on in any subsequent transfer.

This does not change the security obligations in Article 37, which still apply.

Unless agreed otherwise (in writing) for specifically-identified third parties or unless impossible under applicable EU and national laws on mergers and acquisitions, a beneficiary that intends to transfer ownership of results must give at least 45 days advance notice (or less if agreed in writing) to the other beneficiaries that still have (or still may request) access rights to the results. This notification must include sufficient information on the new owner to enable any beneficiary concerned to assess the effects on its access rights.

Unless agreed otherwise (in writing) for specifically-identified third parties, any other beneficiary may object within 30 days of receiving notification (or less if agreed in writing), if it can show that the transfer would adversely affect its access rights. In this case, the transfer may not take place until agreement has been reached between the beneficiaries concerned.

30.2 Granting licenses

Each beneficiary may grant licences to its results (or otherwise give the right to exploit them), if:

(a) this does not impede the access rights under Article 31 and

(b) not applicable.

In addition to Points (a) and (b), exclusive licences for results may be granted only if all the other beneficiaries concerned have waived their access rights (see Article 31.1).

This does not change the dissemination obligations in Article 29 or security obligations in Article 37, which still apply.

30.3 Commission right to object to transfers or licensing

Not applicable

30.4 Consequences of non-compliance
If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

**ARTICLE 31 — ACCESS RIGHTS TO RESULTS**

**31.1 Exercise of access rights — Waiving of access rights — No sub-licensing**

The conditions set out in Article 25.1 apply.

The obligations set out in this Article do not change the security obligations in Article 37, which still apply.

**31.2 Access rights for other beneficiaries, for implementing their own tasks under the action**

The beneficiaries must give each other access — on a royalty-free basis — to results needed for implementing their own tasks under the action.

**31.3 Access rights for other beneficiaries, for exploiting their own results**

The beneficiaries must give each other — under fair and reasonable conditions (see Article 25.3) — access to results needed for exploiting their own results.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

**31.4 Access rights of affiliated entities**

Unless agreed otherwise in the consortium agreement, access to results must also be given — under fair and reasonable conditions (Article 25.3) — to affiliated entities established in an EU Member State or associated country, if this is needed for those entities to exploit the results generated by the beneficiaries to which they are affiliated.

Unless agreed otherwise (see above; Article 31.1), the affiliated entity concerned must make any such request directly to the beneficiary that owns the results.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

**31.5 Access rights for the EU institutions, bodies, offices or agencies and EU Member States**

The beneficiaries must give access to their results — on a royalty-free basis — to EU institutions, bodies, offices or agencies, for developing, implementing or monitoring EU policies or programmes.

Such access rights are limited to non-commercial and non-competitive use.

This does not change the right to use any material, document or information received from the beneficiaries for communication and publicising activities (see Article 38.2).

**31.6 Access rights for third parties**
31.7 **Consequences of non-compliance**

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

**SECTION 4 OTHER RIGHTS AND OBLIGATIONS**

**ARTICLE 32 — RECRUITMENT AND WORKING CONDITIONS FOR RESEARCHERS**

**32.1 Obligation to take measures to implement the European Charter for Researchers and Code of Conduct for the Recruitment of Researchers**

The beneficiaries must take all measures to implement the principles set out in the Commission Recommendation on the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers\(^\text{23}\), in particular regarding:

- working conditions;
- transparent recruitment processes based on merit, and
- career development.

The beneficiaries must ensure that researchers and third parties involved in the action are aware of them.

**32.2 Consequences of non-compliance**

If a beneficiary breaches its obligations under this Article, the Commission may apply any of the measures described in Chapter 6.

**ARTICLE 33 — GENDER EQUALITY**

**33.1 Obligation to aim for gender equality**

The beneficiaries must take all measures to promote equal opportunities between men and women in the implementation of the action. They must aim, to the extent possible, for a gender balance at all levels of personnel assigned to the action, including at supervisory and managerial level.

**33.2 Consequences of non-compliance**

If a beneficiary breaches its obligations under this Article, the Commission may apply any of the measures described in Chapter 6.

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ARTICLE 34 — ETHICS AND RESEARCH INTEGRITY

34.1 Obligation to comply with ethical and research integrity principles

The beneficiaries must carry out the action in compliance with:

(a) ethical principles (including the highest standards of research integrity) and

(b) applicable international, EU and national law.

Funding will not be granted for activities carried out outside the EU if they are prohibited in all Member States or for activities which destroy human embryos (for example, for obtaining stem cells).

The beneficiaries must ensure that the activities under the action have an exclusive focus on civil applications.

The beneficiaries must ensure that the activities under the action do not:

(a) aim at human cloning for reproductive purposes;

(b) intend to modify the genetic heritage of human beings which could make such changes heritable (with the exception of research relating to cancer treatment of the gonads, which may be financed), or

(c) intend to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer.

In addition, the beneficiaries must respect the fundamental principle of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity24.

This implies compliance with the following fundamental principles:

- **reliability** in ensuring the quality of research reflected in the design, the methodology, the analysis and the use of resources;

- **honesty** in developing, undertaking, reviewing, reporting and communicating research in a transparent, fair and unbiased way;

- **respect** for colleagues, research participants, society, ecosystems, cultural heritage and the environment;

- **accountability** for the research from idea to publication, for its management and organisation, for training, supervision and mentoring, and for its wider impacts

and means that beneficiaries must ensure that persons carrying out research tasks follow the good research practices and refrain from the research integrity violations described in this Code.

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24 European Code of Conduct for Research Integrity of ALLEA (All European Academies)
This does not change the other obligations under this Agreement or obligations under applicable international, EU or national law, all of which still apply.

34.2 Activities raising ethical issues

Activities raising ethical issues must comply with the ‘ethics requirements’ set out as deliverables in Annex 1.

Before the beginning of an activity raising an ethical issue, each beneficiary must have obtained:

(a) any ethics committee opinion required under national law and

(b) any notification or authorisation for activities raising ethical issues required under national and/or European law

needed for implementing the action tasks in question.

The documents must be kept on file and be submitted upon request by the coordinator to the Commission (see Article 52). If they are not in English, they must be submitted together with an English summary, which shows that the action tasks in question are covered and includes the conclusions of the committee or authority concerned (if available).

34.3 Activities involving human embryos or human embryonic stem cells

Activities involving research on human embryos or human embryonic stem cells may be carried out, in addition to Article 34.1, only if:

- they are set out in Annex 1 or

- the coordinator has obtained explicit approval (in writing) from the Commission (see Article 52).

34.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or participation of the beneficiary may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 35 — CONFLICT OF INTERESTS

35.1 Obligation to avoid a conflict of interests

The beneficiaries must take all measures to prevent any situation where the impartial and objective implementation of the action is compromised for reasons involving economic interest, political or national affinity, family or emotional ties or any other shared interest (‘conflict of interests’).

They must formally notify to the Commission without delay any situation constituting or likely to lead to a conflict of interests and immediately take all the necessary steps to rectify this situation.

The Commission may verify that the measures taken are appropriate and may require additional measures to be taken by a specified deadline.
35.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or participation of the beneficiary may be terminated (see Article 50). Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 36 — CONFIDENTIALITY

36.1 General obligation to maintain confidentiality

During implementation of the action and for four years after the period set out in Article 3, the parties must keep confidential any data, documents or other material (in any form) that is identified as confidential at the time it is disclosed (‘confidential information’).

If a beneficiary requests, the Commission may agree to keep such information confidential for an additional period beyond the initial four years.

If information has been identified as confidential only orally, it will be considered to be confidential only if this is confirmed in writing within 15 days of the oral disclosure.

Unless otherwise agreed between the parties, they may use confidential information only to implement the Agreement.

The beneficiaries may disclose confidential information to their personnel or third parties involved in the action only if they:

(a) need to know to implement the Agreement and

(b) are bound by an obligation of confidentiality.

This does not change the security obligations in Article 37, which still apply.

The Commission may disclose confidential information to its staff, other EU institutions and bodies. It may disclose confidential information to third parties, if:

(a) this is necessary to implement the Agreement or safeguard the EU’s financial interests and

(b) the recipients of the information are bound by an obligation of confidentiality.

Under the conditions set out in Article 4 of the Rules for Participation Regulation No 1290/2013, the Commission must moreover make available information on the results to other EU institutions, bodies, offices or agencies as well as Member States or associated countries.

The confidentiality obligations no longer apply if:

(a) the disclosing party agrees to release the other party;

(b) the information was already known by the recipient or is given to him without obligation of confidentiality by a third party that was not bound by any obligation of confidentiality;

(c) the recipient proves that the information was developed without the use of confidential information;

(d) the information becomes generally and publicly available, without breaching any confidentiality obligation, or

(e) the disclosure of the information is required by EU or national law.

36.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 37 — SECURITY-RELATED OBLIGATIONS

37.1 Results with a security recommendation

Not applicable

37.2 Classified information

Not applicable

37.3 Activities involving dual-use goods or dangerous materials and substances

Not applicable

37.4 Consequences of non-compliance

Not applicable

ARTICLE 38 — PROMOTING THE ACTION — VISIBILITY OF EU FUNDING

38.1 Communication activities by beneficiaries

38.1.1 Obligation to promote the action and its results

The beneficiaries must promote the action and its results, by providing targeted information to multiple audiences (including the media and the public) in a strategic and effective manner.

This does not change the dissemination obligations in Article 29, the confidentiality obligations in Article 36 or the security obligations in Article 37, all of which still apply.

Before engaging in a communication activity expected to have a major media impact, the beneficiaries must inform the Commission (see Article 52).

38.1.2 Information on EU funding — Obligation and right to use the EU emblem
Unless the Commission requests or agrees otherwise or unless it is impossible, any communication activity related to the action (including in electronic form, via social media, etc.) and any infrastructure, equipment and major results funded by the grant must:

(a) display the EU emblem and

(b) include the following text:

For communication activities:

“This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 101003589”.

For infrastructure, equipment and major results:

“This [infrastructure][equipment][insert type of result] is part of a project that has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 101003589”.

When displayed together with another logo, the EU emblem must have appropriate prominence.

For the purposes of their obligations under this Article, the beneficiaries may use the EU emblem without first obtaining approval from the Commission.

This does not, however, give them the right to exclusive use.

Moreover, they may not appropriate the EU emblem or any similar trademark or logo, either by registration or by any other means.

38.1.3 Disclaimer excluding Commission responsibility

Any communication activity related to the action must indicate that it reflects only the author’s view and that the Commission is not responsible for any use that may be made of the information it contains.

38.2 Communication activities by the Commission

38.2.1 Right to use beneficiaries’ materials, documents or information

The Commission may use, for its communication and publicising activities, information relating to the action, documents notably summaries for publication and public deliverables as well as any other material, such as pictures or audio-visual material received from any beneficiary (including in electronic form).

This does not change the confidentiality obligations in Article 36 and the security obligations in Article 37, all of which still apply.

If the Commission’s use of these materials, documents or information would risk compromising legitimate interests, the beneficiary concerned may request the Commission not to use it (see Article 52).

The right to use a beneficiary’s materials, documents and information includes:

(a) use for its own purposes (in particular, making them available to persons working for the Commission or any other EU institution, body, office or agency or body or institutions in EU Member States; and copying or reproducing them in whole or in part, in unlimited numbers);
(b) **distribution to the public** (in particular, publication as hard copies and in electronic or digital format, publication on the internet, as a downloadable or non-downloadable file, broadcasting by any channel, public display or presentation, communicating through press information services, or inclusion in widely accessible databases or indexes);

(c) **editing or redrafting** for communication and publicising activities (including shortening, summarising, inserting other elements (such as meta-data, legends, other graphic, visual, audio or text elements), extracting parts (e.g. audio or video files), dividing into parts, use in a compilation);

(d) translation;

(e) giving **access in response to individual requests** under Regulation No 1049/2001\(^{27}\), without the right to reproduce or exploit;

(f) **storage** in paper, electronic or other form;

(g) **archiving**, in line with applicable document-management rules, and

(h) the right to authorise **third parties** to act on its behalf or sub-license the modes of use set out in Points (b), (c), (d) and (f) to third parties if needed for the communication and publicising activities of the Commission.

If the right of use is subject to rights of a third party (including personnel of the beneficiary), the beneficiary must ensure that it complies with its obligations under this Agreement (in particular, by obtaining the necessary approval from the third parties concerned).

Where applicable (and if provided by the beneficiaries), the Commission will insert the following information:

“© – [year] – [name of the copyright owner]. All rights reserved. Licensed to the European Union (EU) under conditions.”

### 38.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

### ARTICLE 39 — PROCESSING OF PERSONAL DATA

#### 39.1 Processing of personal data by the Commission

Any personal data under the Agreement will be processed by the Commission under Regulation No 45/2001\(^{28}\) and according to the ‘notifications of the processing operations’ to the Data Protection Officer (DPO) of the Commission (publicly accessible in the DPO register).

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Such data will be processed by the ‘data controller’ of the Commission for the purposes of implementing, managing and monitoring the Agreement or protecting the financial interests of the EU or Euratom (including checks, reviews, audits and investigations; see Article 22).

The persons whose personal data are processed have the right to access and correct their own personal data. For this purpose, they must send any queries about the processing of their personal data to the data controller, via the contact point indicated in the privacy statement(s) that are published on the Commission websites.

They also have the right to have recourse at any time to the European Data Protection Supervisor (EDPS).

39.2 Processing of personal data by the beneficiaries

The beneficiaries must process personal data under the Agreement in compliance with applicable EU and national law on data protection (including authorisations or notification requirements).

The beneficiaries may grant their personnel access only to data that is strictly necessary for implementing, managing and monitoring the Agreement.

The beneficiaries must inform the personnel whose personal data are collected and processed by the Commission. For this purpose, they must provide them with the privacy statement(s) (see above), before transmitting their data to the Commission.

39.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under Article 39.2, the Commission may apply any of the measures described in Chapter 6.

ARTICLE 40 — ASSIGNMENTS OF CLAIMS FOR PAYMENT AGAINST THE COMMISSION

The beneficiaries may not assign any of their claims for payment against the Commission to any third party, except if approved by the Commission on the basis of a reasoned, written request by the coordinator (on behalf of the beneficiary concerned).

If the Commission has not accepted the assignment or the terms of it are not observed, the assignment will have no effect on it.

In no circumstances will an assignment release the beneficiaries from their obligations towards the Commission.

CHAPTER 5 DIVISION OF BENEFICIARIES’ ROLES AND RESPONSIBILITIES — RELATIONSHIP WITH COMPLEMENTARY BENEFICIARIES — RELATIONSHIP WITH PARTNERS OF A JOINT ACTION

of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data (OJ L 8, 12.01.2001, p. 1).
ARTICLE 41 — DIVISION OF BENEFICIARIES’ ROLES AND RESPONSIBILITIES — RELATIONSHIP WITH COMPLEMENTARY BENEFICIARIES — RELATIONSHIP WITH PARTNERS OF A JOINT ACTION

41.1 Roles and responsibility towards the Commission

The beneficiaries have full responsibility for implementing the action and complying with the Agreement.

The beneficiaries are jointly and severally liable for the technical implementation of the action as described in Annex 1. If a beneficiary fails to implement its part of the action, the other beneficiaries become responsible for implementing this part (without being entitled to any additional EU funding for doing so), unless the Commission expressly relieves them of this obligation.

The financial responsibility of each beneficiary is governed by Article 44.

41.2 Internal division of roles and responsibilities

The internal roles and responsibilities of the beneficiaries are divided as follows:

(a) Each beneficiary must:

(i) keep information stored in the Participant Portal Beneficiary Register (via the electronic exchange system) up to date (see Article 17);

(ii) inform the coordinator immediately of any events or circumstances likely to affect significantly or delay the implementation of the action (see Article 17);

(iii) submit to the coordinator in good time:

- individual financial statements for itself and its linked third parties and, if required, certificates on the financial statements (see Article 20);

- the data needed to draw up the technical reports (see Article 20);

- ethics committee opinions and notifications or authorisations for activities raising ethical issues (see Article 34);

- any other documents or information required by the Commission under the Agreement, unless the Agreement requires the beneficiary to submit this information directly to the Commission.

(b) The coordinator must:

(i) monitor that the action is implemented properly (see Article 7);

(ii) act as the intermediary for all communications between the beneficiaries and the Commission (in particular, providing the Commission with the information described in Article 17), unless the Agreement specifies otherwise;

(iii) request and review any documents or information required by the Commission and verify their completeness and correctness before passing them on to the Commission;
(iv) submit the deliverables and reports to the Commission (see Articles 19 and 20);

(v) ensure that all payments are made to the other beneficiaries without unjustified delay (see Article 21);

(vi) inform the Commission of the amounts paid to each beneficiary, when required under the Agreement (see Articles 44 and 50) or requested by the Commission.

The coordinator may not delegate or subcontract the above-mentioned tasks to any other beneficiary or third party (including linked third parties).

41.3 Internal arrangements between beneficiaries — Consortium agreement

The beneficiaries must have internal arrangements regarding their operation and co-ordination to ensure that the action is implemented properly. These internal arrangements must be set out in a written ‘consortium agreement’ between the beneficiaries, which may cover:

- internal organisation of the consortium;
- management of access to the electronic exchange system;
- distribution of EU funding;
- additional rules on rights and obligations related to background and results (including whether access rights remain or not, if a beneficiary is in breach of its obligations) (see Section 3 of Chapter 4);
- settlement of internal disputes;
- liability, indemnification and confidentiality arrangements between the beneficiaries.

The consortium agreement must not contain any provision contrary to the Agreement.

41.4 Relationship with complementary beneficiaries — Collaboration agreement

Not applicable

41.5 Relationship with partners of a joint action — Coordination agreement

Not applicable

CHAPTER 6 REJECTION OF COSTS — REDUCTION OF THE GRANT — RECOVERY — SANCTIONS — DAMAGES — SUSPENSION — TERMINATION — FORCE MAJEURE

SECTION 1 REJECTION OF COSTS — REDUCTION OF THE GRANT — RECOVERY — SANCTIONS

ARTICLE 42 — REJECTION OF INELIGIBLE COSTS
42.1 Conditions

The Commission will — after termination of the participation of a beneficiary, at the time of an interim payment, at the payment of the balance or afterwards — reject any costs which are ineligible (see Article 6), in particular following checks, reviews, audits or investigations (see Article 22).

The rejection may also be based on the extension of findings from other grants to this grant (see Article 22.5.2).

42.2 Ineligible costs to be rejected — Calculation — Procedure

Ineligible costs will be rejected in full.

If the rejection of costs does not lead to a recovery (see Article 44), the Commission will formally notify the coordinator or beneficiary concerned of the rejection of costs, the amounts and the reasons why (if applicable, together with the notification of amounts due; see Article 21.5). The coordinator or beneficiary concerned may — within 30 days of receiving notification — formally notify the Commission of its disagreement and the reasons why.

If the rejection of costs leads to a recovery, the Commission will follow the contradictory procedure with pre-information letter set out in Article 44.

42.3 Effects

If the Commission rejects costs at the time of an interim payment or the payment of the balance, it will deduct them from the total eligible costs declared, for the action, in the periodic or final summary financial statement (see Articles 20.3 and 20.4). It will then calculate the interim payment or payment of the balance as set out in Articles 21.3 or 21.4.

If the Commission rejects costs after termination of the participation of a beneficiary, it will deduct them from the costs declared by the beneficiary in the termination report and include the rejection in the calculation after termination (see Article 50.2 and 50.3).

If the Commission — after an interim payment but before the payment of the balance — rejects costs declared in a periodic summary financial statement, it will deduct them from the total eligible costs declared, for the action, in the next periodic summary financial statement or in the final summary financial statement. It will then calculate the interim payment or payment of the balance as set out in Articles 21.3 or 21.4.

If the Commission rejects costs after the payment of the balance, it will deduct the amount rejected from the total eligible costs declared, by the beneficiary, in the final summary financial statement. It will then calculate the revised final grant amount as set out in Article 5.4.

ARTICLE 43 — REDUCTION OF THE GRANT

43.1 Conditions

The Commission may — after termination of the participation of a beneficiary, at the payment of the balance or afterwards — reduce the grant amount (see Article 5.1), if:
(a) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed:

(i) substantial errors, irregularities or fraud or

(ii) serious breach of obligations under the Agreement or during the award procedure (including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles) or

(b) a beneficiary (or a natural person who has the power to represent or take decision on its behalf) has committed — in other EU or Euratom grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (extension of findings from other grants to this grant; see Article 22.5.2).

43.2 Amount to be reduced — Calculation — Procedure

The amount of the reduction will be proportionate to the seriousness of the errors, irregularities or fraud or breach of obligations.

Before reduction of the grant, the Commission will formally notify a ‘pre-information letter’ to the coordinator or beneficiary concerned:

- informing it of its intention to reduce the grant, the amount it intends to reduce and the reasons why and

- inviting it to submit observations within 30 days of receiving notification.

If the Commission does not receive any observations or decides to pursue reduction despite the observations it has received, it will formally notify confirmation of the reduction (if applicable, together with the notification of amounts due; see Article 21).

43.3 Effects

If the Commission reduces the grant after termination of the participation of a beneficiary, it will calculate the reduced grant amount for that beneficiary and then determine the amount due to that beneficiary (see Article 50.2 and 50.3).

If the Commission reduces the grant at the payment of the balance, it will calculate the reduced grant amount for the action and then determine the amount due as payment of the balance (see Articles 5.3.4 and 21.4).

If the Commission reduces the grant after the payment of the balance, it will calculate the revised final grant amount for the beneficiary concerned (see Article 5.4). If the revised final grant amount for the beneficiary concerned is lower than its share of the final grant amount, the Commission will recover the difference (see Article 44).

ARTICLE 44 — RECOVERY OF UNDUE AMOUNTS

44.1 Amount to be recovered — Calculation — Procedure

The Commission will — after termination of the participation of a beneficiary, at the payment
of the balance or afterwards — claim back any amount that was paid, but is not due under the Agreement.

Each beneficiary’s financial responsibility in case of recovery is limited to its own debt (including undue amounts paid by the Commission for costs declared by its linked third parties), except for the amount retained for the Guarantee Fund (see Article 21.4).

44.1.1 Recovery after termination of a beneficiary’s participation

If recovery takes place after termination of a beneficiary’s participation (including the coordinator), the Commission will claim back the undue amount from the beneficiary concerned, by formally notifying it a debit note (see Article 50.2 and 50.3). This note will specify the amount to be recovered, the terms and the date for payment.

If payment is not made by the date specified in the debit note, the Commission will recover the amount:

(a) by ‘offsetting’ it — without the beneficiary’s consent — against any amounts owed to the beneficiary concerned by the Commission or an executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU’s financial interests, the Commission may offset before the payment date specified in the debit note;

(b) not applicable;

(c) by taking legal action (see Article 57) or by adopting an enforceable decision under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date specified in the debit note, the amount to be recovered (see above) will be increased by late-payment interest at the rate set out in Article 21.11, from the day following the payment date in the debit note, up to and including the date the Commission receives full payment of the amount.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2007/64/EC applies.

44.1.2 Recovery at payment of the balance

If the payment of the balance takes the form of a recovery (see Article 21.4), the Commission will formally notify a ‘pre-information letter’ to the coordinator:

- informing it of its intention to recover, the amount due as the balance and the reasons why;

---

specifying that it intends to deduct the amount to be recovered from the amount retained for the Guarantee Fund;

- requesting the coordinator to submit a report on the distribution of payments to the beneficiaries within 30 days of receiving notification, and

- inviting the coordinator to submit observations within 30 days of receiving notification.

If no observations are submitted or the Commission decides to pursue recovery despite the observations it has received, it will confirm recovery (together with the notification of amounts due; see Article 21.5) and:

- pay the difference between the amount to be recovered and the amount retained for the Guarantee Fund, if the difference is positive or

- formally notify to the coordinator a debit note for the difference between the amount to be recovered and the amount retained for the Guarantee Fund, if the difference is negative. This note will also specify the terms and the date for payment.

If the coordinator does not repay the Commission by the date in the debit note and has not submitted the report on the distribution of payments: the Commission will recover the amount set out in the debit note from the coordinator (see below).

If the coordinator does not repay the Commission by the date in the debit note, but has submitted the report on the distribution of payments: the Commission will:

(a) identify the beneficiaries for which the amount calculated as follows is negative:

\[
\frac{\{\text{beneficiary’s costs declared in the final summary financial statement and approved by the Commission multiplied by the reimbursement rate set out in Article 5.2 for the beneficiary concerned} \\
\quad \text{plus} \\
\quad \text{its linked third parties’ costs declared in the final summary financial statement and approved by the Commission multiplied by the reimbursement rate set out in Article 5.2 for each linked third party concerned}\} \\
\quad \text{divided by} \\
\quad \text{the EU contribution for the action calculated according to Article 5.3.1}\} \\
\quad \text{multiplied by} \\
\quad \text{the final grant amount (see Article 5.3)} \\
\quad \text{minus} \\
\quad \{\text{pre-financing and interim payments received by the beneficiary}\}}
\]

(b) formally notify to each beneficiary identified according to point (a) a debit note specifying the terms and date for payment. The amount of the debit note is calculated as follows:

\[
\left\{\frac{\{\text{amount calculated according to point (a) for the beneficiary concerned} \\
\quad \text{divided by} \\
\quad \text{proportion}\}}\right\}
\]
the sum of the amounts calculated according to point (a) for all the beneficiaries identified according to point (a)
multiplied by
the amount set out in the debit note formally notified to the coordinator}.

If payment is not made by the date specified in the debit note, the Commission will **recover** the amount:

(a) by **offsetting** it — without the beneficiary’s consent — against any amounts owed to the beneficiary concerned by the Commission or an executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU’s financial interests, the Commission may offset before the payment date specified in the debit note;

(b) by **drawing on the Guarantee Fund**. The Commission will formally notify the beneficiary concerned the debit note on behalf of the Guarantee Fund and recover the amount:

(i) not applicable;

(ii) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the payment date in the debit note, up to and including the date the Commission receives full payment of the amount.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2007/64/EC applies.

**44.1.3 Recovery of amounts after payment of the balance**

If, for a beneficiary, the revised final grant amount (see Article 5.4) is lower than its share of the final grant amount, it must repay the difference to the Commission.

The beneficiary’s share of the final grant amount is calculated as follows:

\[
\left\{\begin{align*}
\text{beneficiary’s costs declared in the final summary financial statement and approved by the Commission multiplied by the reimbursement rate set out in Article 5.2 for the beneficiary concerned} \\
\text{plus} \\
\text{its linked third parties’ costs declared in the final summary financial statement and approved by the Commission multiplied by the reimbursement rate set out in Article 5.2 for each linked third party concerned} \\
\text{divided by} \\
\text{the EU contribution for the action calculated according to Article 5.3.1}
\end{align*}\right.
\]
multiplied by
the final grant amount (see Article 5.3).

If the coordinator has not distributed amounts received (see Article 21.7), the Commission will also recover these amounts.

The Commission will formally notify a pre-information letter to the beneficiary concerned:
- informing it of its intention to recover, the due amount and the reasons why and
- inviting it to submit observations within 30 days of receiving notification.

If no observations are submitted or the Commission decides to pursue recovery despite the observations it has received, it will confirm the amount to be recovered and formally notify to the beneficiary concerned a debit note. This note will also specify the terms and the date for payment.

If payment is not made by the date specified in the debit note, the Commission will recover the amount:

(a) by offsetting it — without the beneficiary’s consent — against any amounts owed to the beneficiary concerned by the Commission or an executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU’s financial interests, the Commission may offset before the payment date specified in the debit note;

(b) by drawing on the Guarantee Fund. The Commission will formally notify the beneficiary concerned the debit note on behalf of the Guarantee Fund and recover the amount:

(i) not applicable;

(ii) by taking legal action (see Article 57) or by adopting an enforceable decision under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date in the debit note, the amount to be recovered (see above) will be increased by late-payment interest at the rate set out in Article 21.11, from the day following the date for payment in the debit note, up to and including the date the Commission receives full payment of the amount.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2007/64/EC applies.

ARTICLE 45 — ADMINISTRATIVE SANCTIONS

In addition to contractual measures, the Commission may also adopt administrative sanctions under Articles 106 and 131(4) of the Financial Regulation No 966/2012 (i.e. exclusion from future procurement contracts, grants, prizes and expert contracts and/or financial penalties).
SECTION 2  LIABILITY FOR DAMAGES

ARTICLE 46 — LIABILITY FOR DAMAGES

46.1 Liability of the Commission

The Commission cannot be held liable for any damage caused to the beneficiaries or to third parties as a consequence of implementing the Agreement, including for gross negligence.

The Commission cannot be held liable for any damage caused by any of the beneficiaries or third parties involved in the action, as a consequence of implementing the Agreement.

46.2 Liability of the beneficiaries

Except in case of force majeure (see Article 51), the beneficiaries must compensate the Commission for any damage it sustains as a result of the implementation of the action or because the action was not implemented in full compliance with the Agreement.

SECTION 3  SUSPENSION AND TERMINATION

ARTICLE 47 — SUSPENSION OF PAYMENT DEADLINE

47.1 Conditions

The Commission may — at any moment — suspend the payment deadline (see Article 21.2 to 21.4) if a request for payment (see Article 20) cannot be approved because:

(a) it does not comply with the provisions of the Agreement (see Article 20);

(b) the technical or financial reports have not been submitted or are not complete or additional information is needed, or

(c) there is doubt about the eligibility of the costs declared in the financial statements and additional checks, reviews, audits or investigations are necessary.

47.2 Procedure

The Commission will formally notify the coordinator of the suspension and the reasons why.

The suspension will take effect the day notification is sent by the Commission (see Article 52).

If the conditions for suspending the payment deadline are no longer met, the suspension will be lifted — and the remaining period will resume.

If the suspension exceeds two months, the coordinator may request the Commission if the suspension will continue.

If the payment deadline has been suspended due to the non-compliance of the technical or financial reports (see Article 20) and the revised report or statement is not submitted or was submitted but is also rejected, the Commission may also terminate the Agreement or the participation of the beneficiary (see Article 50.3.1(l)).
ARTICLE 48 — SUSPENSION OF PAYMENTS

48.1 Conditions

The Commission may — at any moment — suspend payments, in whole or in part and interim payments or the payment of the balance for one or more beneficiaries, if:

(a) a beneficiary (or a natural person who has the power to represent or take decision on its behalf) has committed or is suspected of having committed:

   (i) substantial errors, irregularities or fraud or
   (ii) serious breach of obligations under the Agreement or during the award procedure (including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles) or

(b) a beneficiary (or a natural person who has the power to represent or take decision on its behalf) has committed — in other EU or Euratom grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (extension of findings from other grants to this grant; see Article 22.5.2).

If payments are suspended for one or more beneficiaries, the Commission will make partial payment(s) for the part(s) not suspended. If suspension concerns the payment of the balance, — once suspension is lifted — the payment or the recovery of the amount(s) concerned will be considered the payment of the balance that closes the action.

48.2 Procedure

Before suspending payments, the Commission will formally notify the coordinator or beneficiary concerned:

- informing it of its intention to suspend payments and the reasons why and

- inviting it to submit observations within 30 days of receiving notification.

If the Commission does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify confirmation of the suspension. Otherwise, it will formally notify that the suspension procedure is not continued.

The suspension will take effect the day the confirmation notification is sent by the Commission.

If the conditions for resuming payments are met, the suspension will be lifted. The Commission will formally notify the coordinator or beneficiary concerned.

During the suspension, the periodic report(s) for all reporting periods except the last one (see Article 20.3), must not contain any individual financial statements from the beneficiary concerned and its linked third parties. The coordinator must include them in the next periodic report after the suspension is lifted or — if suspension is not lifted before the end of the action — in the last periodic report.
The beneficiaries may suspend implementation of the action (see Article 49.1) or terminate the Agreement or the participation of the beneficiary concerned (see Article 50.1 and 50.2).

ARTICLE 49 — SUSPENSION OF THE ACTION IMPLEMENTATION

49.1 Suspension of the action implementation, by the beneficiaries

49.1.1 Conditions

The beneficiaries may suspend implementation of the action or any part of it, if exceptional circumstances — in particular force majeure (see Article 51) — make implementation impossible or excessively difficult.

49.1.2 Procedure

The coordinator must immediately formally notify to the Commission the suspension (see Article 52), stating:

- the reasons why and
- the expected date of resumption.

The suspension will take effect the day this notification is received by the Commission.

Once circumstances allow for implementation to resume, the coordinator must immediately formally notify the Commission and request an amendment of the Agreement to set the date on which the action will be resumed, extend the duration of the action and make other changes necessary to adapt the action to the new situation (see Article 55) — unless the Agreement or the participation of a beneficiary has been terminated (see Article 50).

The suspension will be lifted with effect from the resumption date set out in the amendment. This date may be before the date on which the amendment enters into force.

Costs incurred during suspension of the action implementation are not eligible (see Article 6).

49.2 Suspension of the action implementation, by the Commission

49.2.1 Conditions

The Commission may suspend implementation of the action or any part of it, if:

(a) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed or is suspected of having committed:

(i) substantial errors, irregularities or fraud or

(ii) serious breach of obligations under the Agreement or during the award procedure (including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles);

(b) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed — in other EU or Euratom grants awarded to it under similar conditions —
systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (extension of findings from other grants to this grant; see Article 22.5.2), or

(c) the action is suspected of having lost its scientific or technological relevance.

49.2.2 Procedure

Before suspending implementation of the action, the Commission will formally notify the coordinator or beneficiary concerned:

- informing it of its intention to suspend the implementation and the reasons why and
- inviting it to submit observations within 30 days of receiving notification.

If the Commission does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify confirmation of the suspension. Otherwise, it will formally notify that the procedure is not continued.

The suspension will take effect five days after confirmation notification is received (or on a later date specified in the notification).

It will be lifted if the conditions for resuming implementation of the action are met.

The coordinator or beneficiary concerned will be formally notified of the lifting and the Agreement will be amended to set the date on which the action will be resumed, extend the duration of the action and make other changes necessary to adapt the action to the new situation (see Article 55) — unless the Agreement has already been terminated (see Article 50).

The suspension will be lifted with effect from the resumption date set out in the amendment. This date may be before the date on which the amendment enters into force.

Costs incurred during suspension are not eligible (see Article 6).

The beneficiaries may not claim damages due to suspension by the Commission (see Article 46).

Suspension of the action implementation does not affect the Commission’s right to terminate the Agreement or participation of a beneficiary (see Article 50), reduce the grant or recover amounts unduly paid (see Articles 43 and 44).

ARTICLE 50 — TERMINATION OF THE AGREEMENT OR OF THE PARTICIPATION OF ONE OR MORE BENEFICIARIES

50.1 Termination of the Agreement, by the beneficiaries

50.1.1 Conditions and procedure

The beneficiaries may terminate the Agreement.

The coordinator must formally notify termination to the Commission (see Article 52), stating:

- the reasons why and
- the date the termination will take effect. This date must be after the notification.

If no reasons are given or if the Commission considers the reasons do not justify termination, the Agreement will be considered to have been ‘terminated improperly’.

The termination will take effect on the day specified in the notification.

50.1.2 Effects

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a periodic report (for the open reporting period until termination; see Article 20.3) and

(ii) the final report (see Article 20.4).

If the Commission does not receive the reports within the deadline (see above), only costs which are included in an approved periodic report will be taken into account.

The Commission will calculate the final grant amount (see Article 5.3) and the balance (see Article 21.4) on the basis of the reports submitted. Only costs incurred until termination are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

Improper termination may lead to a reduction of the grant (see Article 43).

After termination, the beneficiaries’ obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38, 40, 42, 43 and 44) continue to apply.

50.2 Termination of the participation of one or more beneficiaries, by the beneficiaries

50.2.1 Conditions and procedure

The participation of one or more beneficiaries may be terminated by the coordinator, on request of the beneficiary concerned or on behalf of the other beneficiaries.

The coordinator must formally notify termination to the Commission (see Article 52) and inform the beneficiary concerned.

If the coordinator’s participation is terminated without its agreement, the formal notification must be done by another beneficiary (acting on behalf of the other beneficiaries).

The notification must include:

- the reasons why;

- the opinion of the beneficiary concerned (or proof that this opinion has been requested in writing);

- the date the termination takes effect. This date must be after the notification, and

- a request for amendment (see Article 55), with a proposal for reallocation of the tasks and the estimated budget of the beneficiary concerned (see Annexes 1 and 2) and, if necessary, the addition of one or more new beneficiaries (see Article 56). If termination takes effect after the period set out in Article 3, no request for amendment must be included unless the beneficiary
concerned is the coordinator. In this case, the request for amendment must propose a new coordinator.

If this information is not given or if the Commission considers that the reasons do not justify termination, the participation will be considered to have been terminated improperly.

The termination will take effect on the day specified in the notification.

50.2.2 Effects

The coordinator must — within 30 days from when termination takes effect — submit:

(i) a report on the distribution of payments to the beneficiary concerned and

(ii) if termination takes effect during the period set out in Article 3, a ‘termination report’ from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, an overview of the use of resources, the individual financial statement and, if applicable, the certificate on the financial statement (see Articles 20.3 and 20.4).

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 20.3).

If the request for amendment is rejected by the Commission (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the Agreement may be terminated according to Article 50.3.1(c).

If the request for amendment is accepted by the Commission, the Agreement is amended to introduce the necessary changes (see Article 55).

The Commission will — on the basis of the periodic reports, the termination report and the report on the distribution of payments — calculate the amount which is due to the beneficiary and if the (pre-financing and interim) payments received by the beneficiary exceed this amount.

The amount which is due is calculated in the following steps:

Step 1 — Application of the reimbursement rate to the eligible costs

The grant amount for the beneficiary is calculated by applying the reimbursement rate(s) to the total eligible costs declared by the beneficiary and its linked third parties in the termination report and approved by the Commission.

Only costs incurred by the beneficiary concerned until termination takes effect are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

Step 2 — Reduction due to substantial errors, irregularities or fraud or serious breach of obligations

In case of a reduction (see Article 43), the Commission will calculate the reduced grant amount for the beneficiary by deducting the amount of the reduction (calculated in proportion to the seriousness of the errors, irregularities or fraud or breach
of obligations, in accordance with Article 43.2) from the grant amount for the beneficiary.

If the payments received **exceed the amounts due:**

- if termination takes effect during the period set out in Article 3 and the request for amendment is accepted, the beneficiary concerned must repay to the coordinator the amount unduly received. The Commission will formally notify the amount unduly received and request the beneficiary concerned to repay it to the coordinator within 30 days of receiving notification. If it does not repay the coordinator, the Commission will draw upon the Guarantee Fund to pay the coordinator and then notify a **debit note** on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

- in all other cases, in particular if termination takes effect after the period set out in Article 3, the Commission will formally notify a **debit note** to the beneficiary concerned. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the Commission the amount due and the Commission will notify a debit note on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

- if the beneficiary concerned is the former coordinator, it must repay the new coordinator according to the procedure above, unless:
  - termination takes effect after an interim payment and
  - the former coordinator has not distributed amounts received as pre-financing or interim payments (see Article 21.7).

In this case, the Commission will formally notify a **debit note** to the former coordinator. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the Commission the amount due. The Commission will then pay the new coordinator and notify a debit note on behalf of the Guarantee Fund to the former coordinator (see Article 44).

If the payments received **do not exceed the amounts due:** amounts owed to the beneficiary concerned will be included in the next interim or final payment.

If the Commission does not receive the termination report within the deadline (see above), only costs included in an approved periodic report will be taken into account.

If the Commission does not receive the report on the distribution of payments within the deadline (see above), it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that

- the beneficiary concerned must not repay any amount to the coordinator.

Improper termination may lead to a reduction of the grant (see Article 43) or termination of the Agreement (see Article 50).

After termination, the concerned beneficiary’s obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38, 40, 42, 43 and 44) continue to apply.
50.3 Termination of the Agreement or the participation of one or more beneficiaries, by the Commission

50.3.1 Conditions

The Commission may terminate the Agreement or the participation of one or more beneficiaries, if:

(a) one or more beneficiaries do not accede to the Agreement (see Article 56);

(b) a change to their legal, financial, technical, organisational or ownership situation (or those of its linked third parties) is likely to substantially affect or delay the implementation of the action or calls into question the decision to award the grant;

(c) following termination of participation for one or more beneficiaries (see above), the necessary changes to the Agreement would call into question the decision awarding the grant or breach the principle of equal treatment of applicants (see Article 55);

(d) implementation of the action is prevented by force majeure (see Article 51) or suspended by the coordinator (see Article 49.1) and either:

   (i) resumption is impossible, or

   (ii) the necessary changes to the Agreement would call into question the decision awarding the grant or breach the principle of equal treatment of applicants;

(e) a beneficiary is declared bankrupt, being wound up, having its affairs administered by the courts, has entered into an arrangement with creditors, has suspended business activities, or is subject to any other similar proceedings or procedures under national law;

(f) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has been found guilty of professional misconduct, proven by any means;

(g) a beneficiary does not comply with the applicable national law on taxes and social security;

(h) the action has lost scientific or technological relevance;

(i) not applicable;

(j) not applicable;

(k) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed fraud, corruption, or is involved in a criminal organisation, money laundering or any other illegal activity;

(l) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed:

   (i) substantial errors, irregularities or fraud or

   (ii) serious breach of obligations under the Agreement or during the award procedure (including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles);
(m) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed — in other EU or Euratom grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (extension of findings from other grants to this grant; see Article 22.5.2);

(n) despite a specific request by the Commission, a beneficiary does not request — through the coordinator — an amendment to the Agreement to end the participation of one of its linked third parties or international partners that is in one of the situations under points (e), (f), (g), (k), (l) or (m) and to reallocate its tasks.

50.3.2 Procedure

Before terminating the Agreement or participation of one or more beneficiaries, the Commission will formally notify the coordinator or beneficiary concerned:

- informing it of its intention to terminate and the reasons why and

- inviting it, within 30 days of receiving notification, to submit observations and — in case of Point (l.ii) above — to inform the Commission of the measures to ensure compliance with the obligations under the Agreement.

If the Commission does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify to the coordinator or beneficiary concerned confirmation of the termination and the date it will take effect. Otherwise, it will formally notify that the procedure is not continued.

The termination will take effect:

- for terminations under Points (b), (c), (e), (g), (h), (j), (l.ii) and (n) above: on the day specified in the notification of the confirmation (see above);

- for terminations under Points (a), (d), (f), (i), (k), (l.i) and (m) above: on the day after the notification of the confirmation is received.

50.3.3 Effects

(a) for termination of the Agreement:

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a periodic report (for the last open reporting period until termination; see Article 20.3) and

(ii) a final report (see Article 20.4).

If the Agreement is terminated for breach of the obligation to submit reports (see Articles 20.8 and 50.3.1(l)), the coordinator may not submit any reports after termination.

If the Commission does not receive the reports within the deadline (see above), only costs which are included in an approved periodic report will be taken into account.

The Commission will calculate the final grant amount (see Article 5.3) and the balance (see
Article 21.4) on the basis of the reports submitted. Only costs incurred until termination takes effect are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

This does not affect the Commission’s right to reduce the grant (see Article 43) or to impose administrative sanctions (Article 45).

The beneficiaries may not claim damages due to termination by the Commission (see Article 46).

After termination, the beneficiaries’ obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38, 40, 42, 43 and 44) continue to apply.

(b) for termination of the participation of one or more beneficiaries:

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a report on the distribution of payments to the beneficiary concerned;

(ii) a request for amendment (see Article 55), with a proposal for reallocation of the tasks and estimated budget of the beneficiary concerned (see Annexes 1 and 2) and, if necessary, the addition of one or more new beneficiaries (see Article 56). If termination is notified after the period set out in Article 3, no request for amendment must be submitted unless the beneficiary concerned is the coordinator. In this case the request for amendment must propose a new coordinator, and

(iii) if termination takes effect during the period set out in Article 3, a termination report from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, an overview of the use of resources, the individual financial statement and, if applicable, the certificate on the financial statement (see Article 20).

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 20.3).

If the request for amendment is rejected by the Commission (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the Agreement may be terminated according to Article 50.3.1(c).

If the request for amendment is accepted by the Commission, the Agreement is amended to introduce the necessary changes (see Article 55).

The Commission will — on the basis of the periodic reports, the termination report and the report on the distribution of payments — calculate the amount which is due to the beneficiary and if the (pre-financing and interim) payments received by the beneficiary exceed this amount.

The amount which is due is calculated in the following steps:

Step 1 — Application of the reimbursement rate to the eligible costs

The grant amount for the beneficiary is calculated by applying the reimbursement rate(s) to the total eligible costs declared by the beneficiary
and its linked third parties in the termination report and approved by the Commission.

Only costs incurred by the beneficiary concerned until termination takes effect (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

Step 2 — Reduction due to substantial errors, irregularities or fraud or serious breach of obligations

In case of a reduction (see Article 43), the Commission will calculate the reduced grant amount for the beneficiary by deducting the amount of the reduction (calculated in proportion to the seriousness of the errors, irregularities or fraud or breach of obligations, in accordance with Article 43.2) from the grant amount for the beneficiary.

If the payments received exceed the amounts due:

- if termination takes effect during the period set out in Article 3 and the request for amendment is accepted, the beneficiary concerned must repay to the coordinator the amount unduly received. The Commission will formally notify the amount unduly received and request the beneficiary concerned to repay it to the coordinator within 30 days of receiving notification. If it does not repay the coordinator, the Commission will draw upon the Guarantee Fund to pay the coordinator and then notify a debit note on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

- in all other cases, in particular if termination takes effect after the period set out in Article 3, the Commission will formally notify a debit note to the beneficiary concerned. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the Commission the amount due and the Commission will notify a debit note on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

- if the beneficiary concerned is the former coordinator, it must repay the new coordinator according to the procedure above, unless:
  - termination takes effect after an interim payment and
  - the former coordinator has not distributed amounts received as pre-financing or interim payments (see Article 21.7).

In this case, the Commission will formally notify a debit note to the former coordinator. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the Commission the amount due. The Commission will then pay the new coordinator and notify a debit note on behalf of the Guarantee Fund to the former coordinator (see Article 44).

If the payments received do not exceed the amounts due: amounts owed to the beneficiary concerned will be included in the next interim or final payment.

If the Commission does not receive the termination report within the deadline (see above), only costs included in an approved periodic report will be taken into account.
If the Commission does not receive the report on the distribution of payments within the
deadline (see above), it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that
- the beneficiary concerned must not repay any amount to the coordinator.

After termination, the concerned beneficiary’s obligations (in particular Articles 20, 22, 23,
Section 3 of Chapter 4, 36, 37, 38, 40, 42, 43 and 44) continue to apply.

SECTION 4  FORCE MAJEURE

ARTICLE 51 — FORCE MAJEURE

‘Force majeure’ means any situation or event that:

- prevents either party from fulfilling their obligations under the Agreement,
- was unforeseeable, exceptional situation and beyond the parties’ control,
- was not due to error or negligence on their part (or on the part of third parties involved in the
  action), and
- proves to be inevitable in spite of exercising all due diligence.

The following cannot be invoked as force majeure:

- any default of a service, defect in equipment or material or delays in making them available,
  unless they stem directly from a relevant case of force majeure,
- labour disputes or strikes, or
- financial difficulties.

Any situation constituting force majeure must be formally notified to the other party without delay,
stating the nature, likely duration and foreseeable effects.

The parties must immediately take all the necessary steps to limit any damage due to force majeure
and do their best to resume implementation of the action as soon as possible.

The party prevented by force majeure from fulfilling its obligations under the Agreement cannot be
considered in breach of them.

CHAPTER 7  FINAL PROVISIONS

ARTICLE 52 — COMMUNICATION BETWEEN THE PARTIES

52.1 Form and means of communication
Communication under the Agreement (information, requests, submissions, ‘formal notifications’, etc.) must:

- be made in writing and
- bear the number of the Agreement.

All communication must be made through the Participant Portal electronic exchange system and using the forms and templates provided there.

If — after the payment of the balance — the Commission finds that a formal notification was not accessed, a second formal notification will be made by registered post with proof of delivery (‘formal notification on paper’). Deadlines will be calculated from the moment of the second notification.

Communications in the electronic exchange system must be made by persons authorised according to the Participant Portal Terms & Conditions. For naming the authorised persons, each beneficiary must have designated — before the signature of this Agreement — a ‘legal entity appointed representative (LEAR)’. The role and tasks of the LEAR are stipulated in his/her appointment letter (see Participant Portal Terms & Conditions).

If the electronic exchange system is temporarily unavailable, instructions will be given on the Commission website.

52.2 Date of communication

Communications are considered to have been made when they are sent by the sending party (i.e. on the date and time they are sent through the electronic exchange system).

Formal notifications through the electronic exchange system are considered to have been made when they are received by the receiving party (i.e. on the date and time of acceptance by the receiving party, as indicated by the time stamp). A formal notification that has not been accepted within 10 days after sending is considered to have been accepted.

Formal notifications on paper sent by registered post with proof of delivery (only after the payment of the balance) are considered to have been made on either:

- the delivery date registered by the postal service or
- the deadline for collection at the post office.

If the electronic exchange system is temporarily unavailable, the sending party cannot be considered in breach of its obligation to send a communication within a specified deadline.

52.3 Addresses for communication

The electronic exchange system must be accessed via the following URL:

https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/myarea/projects

The Commission will formally notify the coordinator and beneficiaries in advance any changes to this URL.
Formal notifications on paper (only after the payment of the balance) addressed to the Commission must be sent to the official mailing address indicated on the Commission’s website.

Formal notifications on paper (only after the payment of the balance) addressed to the beneficiaries must be sent to their legal address as specified in the Participant Portal Beneficiary Register.

ARTICLE 53 — INTERPRETATION OF THE AGREEMENT

53.1 Precedence of the Terms and Conditions over the Annexes

The provisions in the Terms and Conditions of the Agreement take precedence over its Annexes.

Annex 2 takes precedence over Annex 1.

53.2 Privileges and immunities

Not applicable

ARTICLE 54 — CALCULATION OF PERIODS, DATES AND DEADLINES

In accordance with Regulation No 1182/71, periods expressed in days, months or years are calculated from the moment the triggering event occurs.

The day during which that event occurs is not considered as falling within the period.

ARTICLE 55 — AMENDMENTS TO THE AGREEMENT

55.1 Conditions

The Agreement may be amended, unless the amendment entails changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

Amendments may be requested by any of the parties.

55.2 Procedure

The party requesting an amendment must submit a request for amendment signed in the electronic exchange system (see Article 52).

The coordinator submits and receives requests for amendment on behalf of the beneficiaries (see Annex 3).

If a change of coordinator is requested without its agreement, the submission must be done by another beneficiary (acting on behalf of the other beneficiaries).

The request for amendment must include:

- the reasons why;

---

- the appropriate supporting documents, and
- for a change of coordinator without its agreement: the opinion of the coordinator (or proof that this opinion has been requested in writing).

The Commission may request additional information.

If the party receiving the request agrees, it must sign the amendment in the electronic exchange system within 45 days of receiving notification (or any additional information the Commission has requested). If it does not agree, it must formally notify its disagreement within the same deadline. The deadline may be extended, if necessary for the assessment of the request. If no notification is received within the deadline, the request is considered to have been rejected.

An amendment enters into force on the day of the signature of the receiving party.

An amendment takes effect on the date agreed by the parties or, in the absence of such an agreement, on the date on which the amendment enters into force.

ARTICLE 56 — ACCESSION TO THE AGREEMENT

56.1 Accession of the beneficiaries mentioned in the Preamble

The other beneficiaries must accede to the Agreement by signing the Accession Form (see Annex 3) in the electronic exchange system (see Article 52) within 30 days after its entry into force (see Article 58).

They will assume the rights and obligations under the Agreement with effect from the date of its entry into force (see Article 58).

If a beneficiary does not accede to the Agreement within the above deadline, the coordinator must — within 30 days — request an amendment to make any changes necessary to ensure proper implementation of the action. This does not affect the Commission’s right to terminate the Agreement (see Article 50).

56.2 Addition of new beneficiaries

In justified cases, the beneficiaries may request the addition of a new beneficiary.

For this purpose, the coordinator must submit a request for amendment in accordance with Article 55. It must include an Accession Form (see Annex 3) signed by the new beneficiary in the electronic exchange system (see Article 52).

New beneficiaries must assume the rights and obligations under the Agreement with effect from the date of their accession specified in the Accession Form (see Annex 3).

ARTICLE 57 — APPLICABLE LAW AND SETTLEMENT OF DISPUTES

57.1 Applicable law

The Agreement is governed by the applicable EU law, supplemented if necessary by the law of Belgium.
57.2 Dispute settlement

If a dispute concerning the interpretation, application or validity of the Agreement cannot be settled amicably, the General Court — or, on appeal, the Court of Justice of the European Union — has sole jurisdiction. Such actions must be brought under Article 272 of the Treaty on the Functioning of the EU (TFEU).

As an exception, if such a dispute is between the Commission and INSTITUT PASTEUR OF SHANGHAI, CHINESE ACADEMY OF SCIENCES, the competent Belgian courts have sole jurisdiction.

If a dispute concerns administrative sanctions, offsetting or an enforceable decision under Article 299 TFEU (see Articles 44, 45 and 46), the beneficiaries must bring action before the General Court — or, on appeal, the Court of Justice of the European Union — under Article 263 TFEU.

ARTICLE 58 — ENTRY INTO FORCE OF THE AGREEMENT

The Agreement will enter into force on the day of signature by the Commission or the coordinator, depending on which is later.

SIGNATURES

For the coordinator

Herman VAN GOETHEM with ECAS id ngeoherm signed in the Participant Portal on 01/04/2020 at 08:57:29 (transaction id SigId-271417-tpPjRTd5BPTR11mJ2rNqg1HyXyzqYDQckTNFmXZosBPzdI7p1lzQj67gyw0k2CQjylazD6vNhHN3N0gGWvxEw-jpJZiczgsw0Ku5x8AwUJVTTm-zGjS1CbxbwsDM7tNwNyKvzswQYyJ1w6OcmdRx1u01LdG). Timestamp by third party at Wed Apr 01 09:57:35 CEST 2020

For the Commission
ANNEX 1 (part A)

Research and Innovation action

NUMBER — 101003589 — RECoVER
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1.1. The project summary

<table>
<thead>
<tr>
<th>Project Number</th>
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**One form per project**

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**Abstract**

RECoVER (Rapid European SARS-CoV-2 Emergency Research response) is a comprehensive research response to the SARS-CoV-2 outbreak addressing the most urgent questions for patient and public health level interventions. RECoVER originates from partners of the EU Framework 7 (FP7) funded PREPARE project (Platform for European Preparedness Against (Re-) emerging Epidemics). In RECoVER, we will address these urgent questions in a comprehensive, multidisciplinary and interacting set of research response activities, combing (i) clinical studies in primary and hospital care, (ii) epidemiological studies and modelling, and (iii) clinical biological studies. The proposed studies complement ongoing research in China, addressing key knowledge gaps and patient-cohort questions relevant to the European population. The research proposed includes essential needs for preparedness and response, even if circulation of the virus in Europe will be limited. RECoVER will inform future research response efforts to further strengthen Europe’s and global clinical research preparedness to future emerging infectious diseases.
## 1.2. List of Beneficiaries

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### 1.3. Workplan Tables - Detailed implementation

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**Total** 304.00
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1.3.3. WT3 Work package descriptions

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**Objectives**

1. To ensure compliance with the EC Grant Agreement and Consortium Agreement, and to ensure that the projects agreed deliverables and milestones are achieved within budget, and on time;
2. To ensure the effective inter-WP alignment of activities and promote efficient and effective internal communication and decision-making;
3. To connect with Public Health agencies (ECDC, WHO, DG SANTE, national agencies), regulatory bodies (EMA, National Competent Authorities), and relevant global initiatives;
4. To disseminate the findings generated in RECOVER using various forms of communication to promote their uptake and ensure optimal impact;
5. To develop our understanding of public perception of risk; public trust in health professionals, in governments, and in science; public willingness to take part in clinical research and public notification and consent preferences.

**Description of work and role of partners**

**WP1 - Management and Impact [Months: 1-24]**

**UANTWERPEN, IP, ERASMUS MC, UOXF, INSERM**

Task 1.1 Consortium coordination and progress monitoring (month 1-24), UA to lead, IP to Co-Lead; all partners involved

Task 1.1 involves the financial-administrative coordination of the project and Consortium. This includes the implementation of the project management structure, decision-making processes and progress monitoring and reporting systems (e.g. installment and facilitation of the project’s management bodies, planning, organisation and follow up of management meetings (governing board, scientific committee), developing a project management manual describing the key processes, roles and responsibilities of the management bodies, coordinating the activities at project level, implementing the decision-making, progress monitoring and reporting processes, monitoring the timely completion of critical milestones, monitoring project-level risks, and developing appropriate risk mitigation measures and the formal coordinating task under the responsibility of the coordinator including the distribution of advance payments and the periodic reporting to the European Commission.

The Governing Board is responsible for the financial and administrative coordination of RECOVER, the alignment of the Work Packages and the decision on escalating the trials in WP2 and WP3. The GB harbours all the lead partners of RECOVER. The GB replaces the SARS-CoV-2 OMC of PREPARE once funded. The GB is advised on scientific matters by the Scientific Committee (SC). The SC includes all lead investigators in RECOVER. The GB and SC are chaired by the coordinator of RECOVER (Herman Goossens) and co-chaired by the scientific coordinator of RECOVER (Sylvie van der Werf). The coordinator is responsible for aligning the activities in PREPARE regarding the SARS-CoV-2 response with those conducted in RECOVER as part of PREPARE’s mode 3 research response.

Task 1.2 Dissemination, Communication and Stakeholder management (month 1-24), UA to lead; UOXF, IP

Building on the communications processes of the PREPARE, COMBACTE, and VALUE-Dx consortium, we will rapidly develop an impact and communications strategy for all research in the RECOVER consortium. The primary aim of the strategy is to ensure that research outcomes reach decision makers managing the public health or clinical response to SARS-CoV-2 in a timely way and in a format that is useful to them in conducting their role. Objectives of the strategy are: (a) to build awareness of RECOVER research among the target “end user” groups; (b) to identify mutual communication pathways at local, national and international levels and preferred communication products for target end users (e.g. policy brief); (c) to ensure that research findings are shared at the earliest point with these end user groups; (d) to track evidence of impact following from research findings.

Task 1.3 Survey of public views on understanding public perception of risk; public trust in governments, and in science; public willingness to take part in clinical research and public notification and consent preferences. (month 1-24), IP or UOXF to Lead; UA
Effective communication to reduce uncertainty and provide clear public health advice is a critical part of the public health response to SARS-CoV-2. Previous studies have identified that public perceptions of risk regarding becoming infected, perceptions of severity of the outbreak and experience of trust impact likelihood of engaging in preventative behaviours. Targeted communication messages are also key to provide clear information about how to seek help and care when a patient is concerned they are infected with SARS-CoV-2. Given that the majority of patients will likely present with mild symptoms, finding ways to mitigate surge demand at community care settings in particular will be important. Home care guidelines are available through WHO, but it is unclear the extent to which messages about home care have penetrated the general public understandings of what to do if they suspect they are unwell with SARS-CoV-2.

Rapid research to understand these aspects in relation to SARS-CoV-2 can provide important information for public health agencies in tailoring communication messages. Further, in previous work we have identified how knowledge about epidemics, and perceptions of trust in government and in health professionals, influence willingness to participate in clinical research. As anticipated, the spread of information about the SARS-CoV-2 epidemic has been accompanied by spread of misinformation. To guide communication strategies and clinical research planning at local and national levels, we propose to conduct a survey among a representative sample of 1000 citizens from each of 8 purposively selected European countries. We will identify 2 countries in each of north, south, east, and west of Europe with confirmed cases of SARS-CoV-2. To rapidly inform research communication strategies for our research partners running the same master protocol for our Intensive Care Unit trial (REMAP-CAP) in other global regions, we will invite other countries (e.g. Canada, Australia and New Zealand) to participate in the survey. The aim of the survey is to understand public perception of risk and of homecare; public trust in governments and in science; public willingness to take part in clinical research and public notification and consent preferences.

We have rapidly re-purposed an existing data collection tool and adapted the accompanying research protocol. We will submit the research protocol to a research ethics committee for rapid review and we anticipate receiving confirmation of ethics waiver, as was the case for previous work of this kind. Ipsos Mori, an international ISO 20252e accredited market research company, will administer the survey. If needed, we will stagger data collection so that data are collected only once there are signs of increasing patient numbers. Respondents voluntarily sign up in advance to an Ipsos Mori question panel, and completion of the questionnaire indicates consent to participate. Age range of respondents will be bounded by Ipsos Mori panel profiles. For most countries we will include participants between 16 and 75 years of age. For respondents under the age of 18 years, Ipsos Mori assures appropriate parental permissions are in place. Respondents are able to refuse to participate in the study at any stage in the process. All data will be processed in accordance with the General Data Protection Regulation. Descriptive analyses will be conducted and regression models will examine associations with outcome variables (engaging in preventative behaviours and participation in clinical research).

This survey can be conducted rapidly and key findings will be shared at the earliest possible point with relevant decision makers. We will identify focal points in public health agencies for whom research findings would be of value and agree communication pathways for rapidly sharing these findings. Research findings will also directly impact our communication strategies including strategies for communicating about the role of clinical research and science in epidemic control.

### Participation per Partner

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Description of deliverables

D1.1 Plan for Dissemination and Communication - Month 1 and continuously updated
D1.2 Communication outputs (policy briefs, press releases, infographics, website) – Month 1 and continuously updated
D1.3 Targeted interim and final policy brief reporting outcomes from the public survey (month 2 -24)
D1.4 : Plan for Dissemination and Communication [3]
RECOVER's dissemination and communication efforts will be targeted at the following stakeholders: Public health authorities and policy makers, health care professionals, wider research community, funders, patients, media. Each group is heterogeneous in its information needs and roles in the SARS-CoV-2 outbreak response. For each group we will design and implement specific dissemination materials and platforms to ensure that the right information reaches the right users in a time-frame relevant to their roles and responsibilities in the SARS-CoV-2 response. RECOVER's dissemination and exploitation strategy will be based on the following principles: - All results will be shared openly as rapidly as possible to the relevant users; - All communications out of will be centrally coordinated with all other networks to ensure coherency of (timing and content of) messaging across PREPARE, VALUE-Dx, COMBACTE and others
D1.5 : Communication outputs [3]
We will share our (preliminary) results with public health authorities, policy makers and healthcare workers via regular policy briefs and healthcare briefs, summarizing our findings in a concise manner. There is a wealth of other research response efforts being implemented by the wider European infectious diseases research response community. Many of our partners working in Europe, but also in regions outside of Europe (e.g. Africa and Asia) have informed
us of their efforts and offered linking their efforts to those conducted in RECOVER. We will reach out to patient organisations such as the International Alliance of Patients’ Organisations (IAPO and European Lung Foundation (ELF) to assess their information needs and how we can best serve these out of RECOVER. RECOVER will target the media with press releases at important time points and milestones. RECOVER’s communication activities include the design of a visual identity, online presence (website, social media...), open access publications, news updates, infographics and brochures.

D1.3 : Policy brief reporting outcomes from the public survey [24]
Interim reports will help guide communication strategies and clinical research planning at local and national levels.

D1.4 : Plan for coordination and collaboration with other SARS-COV-2 projects [3]
Report to include plan for regular meetings to update on each other’s progress, concrete plan on use of common protocols and to ensure harmonization of data collection and coordinated modelling, establishment of inter-project working groups, plan on integration of social sciences capacities and sharing research findings on the dedicated platform (Health Policy Platform/research for policy action).

D1.5 : Interim activity report [6]
Early report on project's progress and activities

D1.6 : Plan for coordination and collaboration with other SARS-COV-2 projects: update 1 [12]
First update of D1.3

D1.7 : Plan for coordination and collaboration with other SARS-COV-2 projects: update 2 [24]
Second update of D1.3

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WP2 involves the Primary care (PC) observational study and community-care perceptions of the novel 2019 coronavirus epidemic. The WP2 studies will build on:

› Our existing PPAS for CA-ARTI in January-March 2020 (VALUE-Dx WP4);
› The experience, protocol, and data capture and management tools used in the PREPARE WP4 ALIC4E trial of neuraminidase inhibitors for influenza-like-illness (the first ever response adaptive platform trial successfully conducted in primary care);
› The IMI/Wellcome planned VALUE-Dx primary care trial, PRUDENCE, testing new POC diagnostics for CA-ARTI and the protocol written and initial organizational steps taken (to start in the winter of 2020-2021)

The overarching objectives of the primary care study are:

› To establish the prevalence (proportion testing positive), disease spectrum, severity and predictors of complications from novel 2019 coronavirus infection (SARS-CoV-2) in primary care in selected European countries;
› To explore primary care patient and primary care healthcare professionals’ perspectives on the coronavirus epidemic in selected European countries;
› To explore the opportunity of testing new point-of-care diagnostics for SARS-CoV-2 in an IMI/Wellcome primary care trial already planned to start in the winter season 2020/21 as part of VALUE-Dx.

Specifically, we will:

› Conduct an enhancement of an ongoing study using ‘fit for purpose’ rigorous methods to capture relevant perceptions of patients regarding help seeking and healthcare professionals about risk, delivery of care and public health messaging during the epidemic itself to inform European and national policy.
› Upgrade our already operative online data capture and management system, Research Online, to include the additional data and report real-time to create a harmonized data-capture and information tool for primary care data for participating European countries.
› Obtain infection prevalence data from up to 20 primary care networks in combination with data from the closest hospital(s) to be used for modelling studies (WP6);
› Link with the VALUE-Dx WP4a PRUDENCE clinical trial that will have the capability to evaluate any new diagnostics that becomes available suitable for testing for CA-ARTI (including SARS-CoV-2) in primary care, to start in the winter 2020/21, which will also recruit in the winter of 2021/22 (funded through VALUE-Dx);

WP2 - Primary care study [Months: 1-24]

UOXF, UANTWERPEN, UMC UTRECHT

Task 2.1: Protocol development (month 0-2): UOXF and UMCU to lead

We will develop a protocol for a prospective, non-randomized observational study of CA-ARTI in primary care in selected European countries during a period of heightened concern about the SARS-CoV-2 (mode 3). This protocol will include capability to register patients with CA-ARTI in primary care in up to 20 countries, capturing data about the presentation, management, risk factors and (reasons for) suspicion for SARS-CoV-2, treatment, routine investigations performed, outcome of tests, taking a throat and/or nasal swab for research purposes, and capturing clinical outcomes and patient and HCP perceptions. Together with UMCU, we will enhance the already operative online data capture and management system with rapid analysis capability for all patient data to be entered, aggregated and analysed, to create a harmonized data-capture tool for primary care data for participating European countries. Our community advisory board is ready to rapidly provide feedback on public facing documents. Outputs will be produced in real time.

› Inclusion criteria: patients presenting in primary care with symptoms or CA-ARTI during the SARS-CoV-2 epidemic in Europe.
› Exclusion criteria: patients who are unable to consent or do not wish to provide informed consent.
› Sampling: one throat and/or nasal swab for all patients stored in universal transport medium, or nasal and separate pharyngeal swab in children.
Primary outcome: prevalence of SARS-CoV-2 in patients presenting primary care during the SARS-CoV-2 epidemic in Europe.

Secondary outcomes: presentation characteristics of SARS-CoV-2 infected patients in primary care and their risk factors for a complicated course of disease, description of variation in care and outcomes, a deep understanding of the relevant perceptions of patients and healthcare professionals to guide health service delivery and public messaging.

Task 2.2: Ethical, Administrative, Regulatory and Legal (EARL) procedures (month 1-6): UMCU to lead

We will rapidly initiate the procedures to gain ethical and other regulatory approvals for this study in up to 20 countries. In parallel, we will establish a process for sampling, storing and transporting samples to the central laboratory, partner 1 UA, and swabs analysis (with WP4), and liaise with local laboratories for faster analysis where appropriate; results will be fed back to responsible clinicians as soon as results are available. Contracts for this work will be established with the local primary care networks. Contracting will be integrated with WP3 and conducted from the University Medical Centre Utrecht (UMCU).

Task 2.3: Patient enrollment and collection of patient data and samples (month 1-24), UMCU and UOXF to lead

We will train the national network facilitators from the selected primary care networks, who will cascade training to their primary care sites in delivering the studies. Sampling materials will be provided by WP4. Patient inclusion will start if/when we enter Mode 3 (widespread infection), as decided by the RECOVER Governing Board.

We do not intend to plan this study with a limit on sample size (of either patients in the prospective observational study, or patients and clinicians in the ‘perceptions’ study), as the required sample to achieve useful descriptions of this condition and to achieve an understanding of the perceptions in primary care will vary as the epidemic evolves, and so the extent and duration of this study will be assessed on a week to week basis. The sample size will also vary according to the need to describe variation in the presentation, management and outcomes not only in individual level, but also by country. Although each network will include a relatively small number of sites, there will be power in pooling these observations and investigate influences of variation in care and health systems on prevalence and outcomes across Europe.

Task 2.4: Data management (month 1 – 24); UMCU to lead

We will use the data collection tools (PPAS in Research Online) developed for the VALUE-Dx study. The form will be adapted to capture protocol adaptations of the PPAS.

Task 2.5: Survey and interviews with healthcare professionals and patients (month 3-24), UA and UOXF to lead

This task will be included in clinical research protocols and ethical approvals will be sought for the protocol as a whole (Task 2.1). In order to rapidly generate evidence for public health and other decision makers, we will include a brief survey for all patients who consent to provide clinical samples. Survey questions will be aligned with those used in the public survey in Task 6.6. Information will be rapidly processed and interim findings fed back to decision makers. Key decision makers will be identified upfront. Pathways for mutual communication and decision-making will be identified with them, during the preparatory phase of the study. In a subset of clinical sites, we will also invite patients and healthcare professionals to participate in an interview:

When patients consent to sampling, we will invite selected patients to participate in a telephone interview planned within 2 weeks after presentation to the clinic to explore their experiences in more depth. Among patients who give their consent to be contacted, we will purposively select patients based on age, gender, symptom presentation, relevant comorbidities and any expressions of concern about SARS-CoV-2 mentioned in their initial consultation. This ‘purposive sampling’ will allow us to achieve a maximum variation sample. Given that the currently identified ‘at risk’ groups involve older patients and those with comorbidities, we will prioritise interviews with these patients. We will also include pregnant women and child patients by doing interviews with parents. We will identify at least one researcher in each country that contributes to this aspect of the research from our existing social science and clinical research networks and rapidly assess and address training needs in recruitment and interviewing approaches. Where feasible, interviewers will be part of the team present in clinics who collect samples and take consent from patients and professionals.

Healthcare professionals will be invited to an interview and purposively selected, where relevant, from those caring for patients presenting with CA-ARTI. We will sample professionals based on job role, any additional responsibilities as a result of SARS-CoV-2 response, years of experience and any specialty training in respiratory medicine and/or response to epidemics. Professionals will be invited to brief interviews after work hours, where workflows allow, or by telephone. We will include receptionists, practice managers, nurses, doctors and other relevant healthcare professionals.

We will seek to carry out interviews with patients during the entire study period and over the course of the evolving pandemic, with data analysis occurring in tandem to inform interview topic guides during the process. Interviews with professionals will occur at the start of the study and may include follow-up interviews with the same participants if there
is a significant change to practice, as a result of SARS-CoV-2, during the study period. Interviews will be carried out in (one of) the local language(s). Interviews will be audio-recorded and transcribed verbatim and translated into English if needed. Transcripts will be analysed using framework analysis and an a priori framework developed to help answer key questions about help-seeking behaviour, delivery of care, perceptions of risk and public health messaging. We will explore differences in patient and professional perceptions and help-seeking and prevention behaviours reported by participants within and across countries.

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## List of deliverables

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### Description of deliverables

D2.1: Approved protocol for the observational study (enhanced PPAS)

This protocol for a prospective, non-randomized observational study of CA-ARTI in primary care will include capability to register patients with CA-ARTI in primary care in up to 20 countries, capturing data about the presentation, management, risk factors and (reasons for) suspicion for SARS-CoV-2, treatment, routine investigations performed, outcome of tests, taking a throat and/or nasal swab for research purposes, and capturing clinical outcomes and patient and HCP perceptions.

D2.2: Upgraded data management system

RECOVER will enhance the already operative online data capture and management system with rapid analysis capability for all patient data to be entered, aggregated and analysed, to create a harmonized data-capture tool for primary care data for participating European countries.

D2.3: Approvals in EU countries, green light for patient inclusions

RECOVER will rapidly initiate the procedures to gain ethical and other regulatory approvals for this study in up to 20 EU and associated countries.

D2.4: Contracts and procedures for sampling, storing and shipment

RECOVER will establish a process for sampling, storing and transporting samples to the central laboratory, partner 1 UA, and swabs’ analysis (with WP4), and liaise with local laboratories for faster analysis where appropriate. Contracts for this work will be established with the local primary care networks. Contracting will be integrated with WP3.

D2.5: UK approved protocol for adapted PRUDENCE trial

RECOVER will seek rapid UK approval of the protocol governing the adapted PRUDENCE trial as originally developed in the VALUE-Dx project.

D2.6: Monthly interim findings from social science related activities

In order to rapidly generate evidence for public health and other decision makers, RECOVER will include a brief survey for patients and healthcare workers. Information will be rapidly processed and interim findings fed back to decision makers.

D2.7: Patients swabs to flow to WP4

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D2.8 : Final study report on clinical data [24]
Final study report on clinical data from the observational study, feeding into WP6

D2.9 : Final study report on social science [24]
Final study report on the social science output

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<td>Approvals in up to 20 EU and associated countries, green-light for patient inclusion.</td>
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<td>Contracts with local laboratories and established procedures for sampling, storing, sending samples to central laboratory.</td>
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The overarching objectives of the hospital care study are:

› To establish the frequency, disease spectrum and severity, clinical features, management, risk factors, spread and outcomes of SARS-CoV-2 infection in hospital care in selected European countries;

› To explore hospital care professionals’ perspectives on the coronavirus epidemic in selected European countries;

› To identify index subjects for contact tracing and household studies that will deliver the samples and data for the biological and modelling studies in WPs 5 and 6;

› To explore opportunities of testing novel diagnostics for SARS-CoV-2 in an IMI/Wellcome funded hospital care trial already planned to start in the winter season 2020/21 as part of VALUE-Dx;

› To explore opportunities of testing new therapeutic agents and/or supportive therapy for severe SARS-CoV-2 infection in the ongoing REMAP-CAP trial as part of PREPARE.

Specifically, we will:

› Rapidly reactivate the MERMAIDS-ARI study in 29 hospitals and 9 primary care networks in Europe;

› Rapidly extend the MERMAIDS-ARI study, named MERMAIDS-ARI 2.0, using our existing, highly functional and already active hospital care network established in the PREPARE, COMBACTE and VALUE-Dx consortia;

› Conduct an ongoing study using ‘fit for purpose’ rigorous methods to capture relevant perceptions of health care professionals and patients about risk, delivery of care and public health messaging during the epidemic itself to inform European and national policy;

› Upgrade our already operative online data capture and management system, Research Online, to include the additional data and report real-time to create a harmonized data-capture and information tool for hospital care data for participating European countries;

› Support the existing, highly functional, and already active REMAP-CAP study;

› Identify index subjects for contact tracing and household studies, for the biological and modelling studies in WPs 5 and 6;

› Link with the VALUE-Dx WP4b clinical trial that will have the capability to evaluate any new diagnostic tests that become available for testing for CA-ARTI (including SARS-CoV-2) in hospital care, to start in the winter 2020/21 and which will also recruit in the winter of 2021/22 (funded through VALUE-Dx).

**WP3 - Hospital care study** [Months: 1-24]

**UMC UTRECHT, UOXF, AMC, PENTA**

The observational Hospital Care study is set-up in two distinguishable parts:

Phase I leverages the network, protocol and procedures applied in the MERMAIDS-ARI observational study on severe ARI to allow for a rapid initiation of the study.

Phase II of WP3 entails the expansion of the number of sites and countries participating to improve geographical coverage in Europe, to enhance accumulation of enrolled cases, to allow more and targeted biological sampling needed for WP 5 and WP6, and to allow enrollment of children (non-eligible in part I). This part is, therefore, named MERMAIDS-ARI 2.0. Part II protocol will be based on the ISARIC-CCP model, aligned to the existing MERMAIDS-ARI protocol, and will allow adaptation, based on evolving scientific insights during the outbreak.

**Tasks**

Task 3.1: Facilitating uniform data collection of the first SARS-CoV-2 infected patients in Europe (month 1-6); UMCU to lead; UOXF, AMC

COMBACTE, through its networks CLIN-Net and LAB-Net, contacted close to 4,000 hospital contacts in 42 countries (on Feb 6, 2020) to use the standardized eCRF developed by ISARIC and endorsed by WHO for anonymized data collection of SARS-CoV-2 infected patients. The COMBACTE website has opened a Frequently Asked Questions part to assist European physicians in organizing this electronic data collection. This activity will be continued.

Task 3.2: Reactivation of MERMAIDS-ARI study sites (month 1-2); UOXF to lead; AMC, UMCU
For Phase I, we will re-implement the protocol for the MERMAIDS-ARI study, a prospective, non-randomised observational study of CA-ARTI in selected European countries. MERMAIDS-ARI enrolled patients presenting to primary care or being hospitalized with an acute respiratory illness. The protocol will be minimally amended to capture additional aspects relevant to SARS-CoV-2 infections, to avoid full IRB revision and new contracts (which would delay start of enrollment). Reactivation includes both the 29 hospitals and the 9 primary care settings. All preparations will start immediately after proposal submission. Reactivation happens within 2 weeks after the decision to enter outbreak response mode 3.

Task 3.3: Protocol development (month 1-2); UMCU to lead
For Phase II, we will adapt the existing MERMAIDS-ARI protocol (part I) to capture additional aspects relevant to SARS-CoV-2 infections, collect more and targeted biological sampling of confirmed SARS-CoV-2 infections needed for WP5 and WP6, and to enroll children (non-eligible in part I). The unified aim of both study parts is to establish the prevalence, disease spectrum and severity, clinical features, management, risk factors, spread and outcomes of SARS-CoV-2 infection in hospital care in European countries. For this purpose, we will align as much as possible with the ISARIC-CCP protocol, with stratified recruitment in tiers of the protocol for subcohorts of patients.

Task 3.4: Selection of new study sites (month 0-2); UMCU to lead
We will actively contact referral hospitals for SARS-CoV-2 in each country for site selection. Having national referrals sites activated in the early stage of the epidemic is particularly attractive, because they will manage the first national SARS-CoV-2 cases. Clinical sites for Phase II will be selected through COMBACTE, VALUE-Dx and PENTA-ID. Site selection will be based on past-performance of study sites in previous COMBACTE studies and geography, to optimize coverage of participating sites across Europe. A feasibility questionnaire will be used to collect site-specific information, such as capability of sites to adhere to ISARIC-CCP protocol specifications, availability of research staff, expected patient numbers and appropriate lab facilities. The procedure of site selection has been developed and used frequently in COMBACTE, and guarantees fast and objective selection of study sites. We will prioritize sites that have on-site SARS-CoV-2 diagnostic capacity available with the possibility of implementing it in routine diagnostic work-up of patients with acute respiratory illness.

Task 3.5: Ethical, Administrative, Regulatory and Legal (EARL) procedures (month 1-5); UMCU to lead
Immediately after proposal submission, we will initiate procedures to gain ethical and other regulatory approval for this study in the countries where clinical sites have been selected. For this, we will benefit from the experiences and procedures developed in COMBACTE and PREPARE.

Task 3.6: Data management (month 1–24); UMCU to lead
We will use the data collection tools (eCRF in Research Online) developed for MERMAIDS-ARI in PREPARE, which will be adapted to capture protocol adaptations made in phase II.

Task 3.7: Conduct of MERMAIDS-ARI (phase I) and MERMAIDS-ARI 2.0 (phase II) (month 1-24); UOXF to lead MERMAIDS-ARI, UMCU to lead MERMAIDS-ARI 2.0
Detailed patient-oriented studies are needed to determine the spectrum of CoVID-19 and the combined influences of age, comorbidities and pathogen co-infections on the development of severe disease. Moreover, the virological and immunological profiles in patients over the course of their disease have yet to be characterized. This research is key to understanding the pathophysiology and epidemiology of this new disease, as well as to identifying potential targets for therapeutic or preventive interventions. The aim of WP3 is to establish an adequately sized cohort of SARS-CoV-2 patients with moderate to severe acute respiratory illness by enrolling sufficient numbers of patients across age-groups, geographic locations, prevalent comorbidities (chronic pulmonary/cardiovascular/metabolic disease) and co-infections.

Design: This is a prospective, multi-center observational study.

Timing: In order to capture the early stages of the epidemic, great effort will be made to initiate patient enrollment as soon as possible. Initial enrollment will take place in activated hospitals sites in Germany, France, Spain and Italy that participated in the MERMAIDS-ARI study (part I), with rapid expansion with sites that are part of the COMBACTE, VALUE-Dx and PENTA-ID Networks (part II, MERMAIDS-ARI 2.0). Our ambition is to be ready for patient enrollment within weeks after proposal submission and to have 30 sites fully operational on July 1st and 50 by month 6. Actual start of enrolling of patients will be determined by the Governing Board, based upon the evolution of the outbreak in Europe. Naturally, start of enrollment can be targeted to regions or countries.

Eligibility: MERMAIDS-ARI: Patients (age 18 years and older) presenting to the Emergency Room or admitted in hospital are eligible for the study if they have a clinical suspicion of a new episode of ARTI. A new episode of acute respiratory illness is defined as 1) sudden onset of self-reported fever or temperature of ≥ 38°C at presentation, 2) at least one respiratory symptom (cough, sore throat, runny or congested nose, dyspnoea) and 3) at least one systemic symptom (headache, muscle ache, sweats or chills or tiredness). Enrollment of patients with CA-ARTI will – when the
outbreak is in Europe - yield patients with SARS-CoV-2 infection and patients with ARTI caused by other pathogens or with no documented etiology. The latter will act as the necessary controls in some of the pursued epidemiological studies. Embedded in MERMAIDS-ARI similar patients will be enrolled in 9 primary care centers in Europe to capture milder illnesses in the same protocol. Of note, this is not part of WP2.

MERMAIDS-ARI 2.0: Patients of all ages presenting to the Emergency Room or admitted in hospital are eligible for the study if they have a documented infection with SARS-CoV-2.

Exclusions: Patients (or legal guardians) not willing/capable to provide informed consent, or patients transferred from another hospital will not be included.

Data and sample collection:
MERMAIDS-ARI: In accordance with current protocol, respiratory and blood (serum, EDTA, blood RNA) specimens will be collected at enrollment from all patients for diagnostic testing (WP4) as well as for laboratory investigations detailed in WP5. Repeat samples will be collected at day 2 or discharge and during convalescence (d28).

MERMAIDS-ARI 2.0: All participating hospitals will keep a weekly screening log of patients eligible for the study. For each patient, a set of non-identifiable data are registered on the log, including gender, age category, results of virological tests and whether the patient was hospitalized/discharged. These logs will be used to monitor the total number of suspected and confirmed SARS-CoV-2 infections presenting to the sites, and this data can be obtained without informed consent. After informed consent has been obtained in patients eligible for study enrollment (i.e. with documented SARS-CoV-2 infection), baseline demographic variables, past medical history, and clinical severity and duration of symptoms, will be registered and entered into the study eCRF. We will follow the ISARIC-CCP protocol, where feasible, with stratified sampling and follow-up schemes by site and patient characteristics. Tier 1 of the scheme includes single biological sampling on Day 1 and clinical information collected at enrollment and discharge. Day one biological sampling includes: 1) respiratory samples (sputum, where available; throat and/or nasal swab culture and PCR to identify viruses and bacteria); 2) a blood sample in EDTA tube. Tier 1 will be implemented in all sites and for all enrolled patients. Tier 2 of the ISARIC-CCP scheme includes serial biological sampling and clinical data collection on Day 1, and then alternate days for the first 2 weeks (if still in hospital), then weekly until resolution of illness or discharge from hospital. In a subgroup of patients follow-up will be extended with a visit at day 28 and recording 90-day mortality. For both Tier 1 and Tier 2, the sampling scheme can be expanded with sampling of additional sites (stool, urine, cerebrospinal fluid, infected body sites) and additional blood samples in serum and blood RNA tubes. Sampling schemes for individual patients will be based on clinical disease course, age of the patient and site participation in data collection for specific diagnostic, virological and immunological studies described in WP4 and 5. Laboratory samples will be labelled with a unique code allocated to each patient at enrollment. An overview of sampling schemes and sites per objective is provided in the table below.

Tier 1 (Single biological sample) - Clinical samples will be collected on enrollment day (Day 1; ideally at initial presentation to a health care facility). Clinical information will be collected at enrollment and discharge.

Tier 2 (Serial biological sampling) - Clinical samples and data will be collected on enrollment day (Day 1; ideally at initial presentation to a health care facility), and then alternate days for the first 2 weeks, then weekly until resolution of illness or discharge from hospital, and again at 3 and 6 months after enrollment.

Sample schemes in WP3 Purpose Task
Serial respiratory, stool, urine and when indicated, CSF samples Quantitative molecular diagnostics, virus isolation and genomic studies 4.6 Exhaustive etiologic diagnosis of the samples collected from patients included in WP2 and WP3
4.7 To correlate viral load in CoV positive patients with severity of disease
5.2 Phenotypic characterization of antigenic, virulence, and possible resistance traits
5.5 Monitor evolution of the epidemic and contribute to the reference database for precision public health
Single or serial blood samples in EDTA Innate and adaptive immune markers 3.10 Identify host risk factors for severe SARS-CoV-2 disease
Serial blood samples in serum- tube Detection of pre-existing cross-reactive antibodies and development of specific antibodies. 5.3 To assess the possible role of prior coronavirus exposures to susceptibility, severity and transmissibility
Single or serial blood samples in RNA tube Host gene expression profiling 5.4 To characterize the host transcriptome in patients with 2019-nCoV in order to understand development of severe disease and identify biomarkers
Sample size: No formal sample size can be calculated as the evolution of the SARS-CoV-2 is highly unpredictable. Instead, we aim to enroll as much patients as possible in order to maximize our power to address the relevant research questions outlined in tasks 3.8-3.10

Task 3.8 Establish the spectrum of disease severity and outcomes of SARS-CoV-2 infections (month 1-24); UMCU and UOXF to lead.

We will analyze all clinically relevant disease outcomes including hospital admission, ICU stay, length of hospital stay, mortality, complications, as well as medical treatments and interventions. Furthermore we will assess frequency, severity and duration of symptoms. Results will be summarized in descriptive statistics and stratified by subgroups of patients based on age, gender, geographic area and comorbidity status. We will compare results for patients infected with 2019-nCoV infections, with other respiratory pathogens and with no pathogen detected. Data collection will be aligned with WP2 (primary care) in order to cover the whole spectrum of disease presentation.

Task 3.9 Quantify severe SARS-CoV-2 infections across age and geographic locations (month 1-24); UMCU and UOXF to lead.

The results of task 3.5 along with the data collected on the weekly screening logs will be used to estimate the total number of severe SARS-CoV-2 infections by region and over time. Adjustments will be made in the estimates for patients with unknown SARS-CoV-2 status. We will use the size of the site-specific catchment population and population census data to estimate incidence rates. Rates will be estimated by age-group and geographic location. Time series will be created to monitor the evolution of the outbreak over time. The results of task 3.7 and WP2 jointly will allow for calculation of the total population disease burden due to mild/moderate and severe SARS-CoV-2 infections.

Task 3.10 Identify host risk factors for severe SARS-CoV-2 disease (CoVID-19) (month 1-24); UMCU and UOXF to lead.

A pre-specified set of potential host risk factors for severe CoVID-19 will be analyzed in multivariate models with several measures of disease outcome as dependent variable. These include, but are not restricted to, hospitalization yes/no, ICU admission, 28-day and 90-day mortality and length of hospital stay. The set of potential risk factors will be based on established risk factors for respiratory (viral and non-viral) infections and on reported potential (or established) risk factors as identified in the early epidemic period in China or elsewhere. In addition to risk factors that can be identified at the time of hospital admission (task 3.7) study outcome from WP5, such as, e.g., viral load, antibody levels, inflammatory markers at the time of admission, will also be included in risk prediction.

Task 3.11 Supporting the REMAP-CAP Platform trial for evaluation of novel therapeutics (month 10-24); UMCU to lead.

Funded through the current PREPARE project until 1/2/2021, we will use the adaptive platform trial (APT) REMAP-CAP of PREPARE for adding new trial arms to evaluate novel therapeutics/ treatment strategies against SARS-CoV-2 infections. It is anticipated that the total number of ICUs in Europe participating in REMAP-CAP will increase from the current 28 to 43 within the funding period of PREPARE. Globally REMAP-CAP currently actively enrolls patients in 52 ICUs in 14 countries (including the 28 ICUs in 10 EU countries) and can adapt new interventions in a flexible manner. These activities, that are an integral part of the Clinical Response Mode 3 of PREPARE, are currently covered by PREPARE funding and will thus be executed in cost-neutral form in RECOVER. New interventions will require separate funding (outside the current budget proposal).

Task 3.12 Exploring opportunities of testing novel diagnostics for 2019-nCoV (month 1-24); UMCU to lead.

We will actively explore to implement scientific evaluation of new diagnostics for SARS-CoV-2, where possible aligning such opportunities with IMI2/Wellcome planned hospital care trial starting in the winter season 2020/21 as part of VALUE-Dx. This will be an individual patient randomized trial to determine the effects of Point of Care testing for atypical bacteria and respiratory virus on patient management (hospitalization yes/no; antibiotics yes/no). The study will be performed in hospitals in South-Eastern Europe, where Point of Care testing is not yet routinely implemented. The hospitals will be prepared for implementing Point of Care testing for SARS-CoV-2 in respiratory samples when available, and will be prioritized for participation in MERMAIDS-ARI 2.0. This will be highly efficient as it integrates the work of this WP3 into an existing planned trial, and will hence be cost-neutral, apart from an additional resource for microbiology testing.

Task 3.13. Rapid survey of health care professionals (month 1-24); UOXF to lead.

Protecting healthcare workers from infection during an epidemic is vital to ensure continuity of clinical care. Effective infection, prevention and control measures are central elements to protecting this workforce and healthcare worker views on the importance of recommended IPC procedures and confidence in enacting them will influence their willingness to follow recommended guidelines. Further, through research with healthcare professionals working during the SARS epidemic, trust in hospital preparedness plans and motivations for continuing to work have been identified as psychological factors that are protective against burnout and post-traumatic stress. Understanding healthcare worker
views can inform hospital strategies for implementing IPC guidelines, inform communication strategies and can inform strategies to protect healthcare worker physical and psychological health. The recent study of Wang et al in JAMA (published online 7 February) showed an alarming rate of hospital-related transmission of 41%. We will rapidly survey staff (doctors, nurses, administrators etc.) working in ER and ICU settings across our hospital networks to assess perceptions of risk, knowledge and views of recommended IPC procedures.

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### Description of deliverables

D3.1 Study protocol MERMAIDS 2.0
D3.2 Data management Plan
D3.3 Site selection procedure for MERMAIDS 2.0
D3.4 Study protocol for survey of healthcare professionals
D3.5 Report of survey of healthcare professionals (pre-outbreak)
D3.6 Study updates/summaries
D3.1 : Study protocol MERMAIDS 2.0 [4]
For Phase II, we will adapt the existing MERMAIDS-ARI protocol (part I) to capture additional aspects relevant to SARS-CoV-2 infections, collect more and targeted biological sampling of confirmed SARS-CoV-2 infections needed for WP5 and WP6, and to enroll children (non-eligible in part I).

D3.2: Site selection procedure for MERMAIDS 2.0 [4]

We will actively contact referral hospitals for SARS-CoV-2 in each country for site selection. Clinical sites for Phase II will be selected through COMBACTE, VALUE-Dx and PENTA-ID. Site selection will be based on past-performance of study sites in previous COMBACTE studies and geography, to optimize coverage of participating sites across Europe. The procedure of site selection has been developed and used frequently in COMBACTE, and guarantees fast and objective selection of study sites. We will prioritize sites that have on-site SARS-CoV-2 diagnostic capacity available with the possibility of implementing it in routine diagnostic work-up of patients with acute respiratory illness (feasibility questionnaire).


Understanding healthcare worker views on the management of the COVID-19 pandemic can inform hospital strategies for implementing IPC guidelines, inform communication strategies and can inform strategies to protect healthcare worker physical and psychological health.


Interview approaches will be pragmatic and adapted to consider the immediate needs of healthcare professionals and to minimise burden.

D3.5: Study updates and summaries [12]

Regular study updates will allow to keep all partners informed about study progress. Dates of 'publication' cannot be specified as patient enrollment depends on the evolution of the pandemic.


Update of the initial draft management plan.

### Schedule of relevant Milestones

<table>
<thead>
<tr>
<th>Milestone number</th>
<th>Milestone title</th>
<th>Lead beneficiary</th>
<th>Due Date (in months)</th>
<th>Means of verification</th>
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<tbody>
<tr>
<td>MS1</td>
<td>Phase I hospital study (MERMAIDS-ARI) initiated</td>
<td>5 - UOXF</td>
<td>1</td>
<td>Initiation of MERMAIDS-ARI hospital study</td>
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<tr>
<td>MS2</td>
<td>Protocol phase II completed</td>
<td>3 - UMC UTRECHT</td>
<td>2</td>
<td>Protocol Phase II MERMAIDS-ARI 2.0 completed</td>
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<tr>
<td>MS3</td>
<td>Phase II study sites selected</td>
<td>3 - UMC UTRECHT</td>
<td>2</td>
<td>New study sites for Phase II study selected</td>
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### Work package number 9

<table>
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<th>WP4</th>
<th>Lead beneficiary</th>
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<tbody>
<tr>
<td>Lab support services</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Start month** 1  
**End month** 24

### Objectives

1. To select through LAB-Net the laboratories supporting clinical trials on the SARS-CoV-2 by the means of creating and sending out a feasibility questionnaire aiming to collect study-specific information in order to facilitate the site selection process;
2. To perform (i) ad-hoc development, validation and deployment of in-house detection assays for SARS-CoV-2, including provision of positive controls and specificity panels, (ii) validation and deployment of second-generation tests (ready-to-use tests) in liaison with the WHO R&D blueprint priority listing;
3. To develop SOPs for standardized and harmonised laboratory-based (in-house) detection of SARS-CoV-2 and other respiratory viruses and bacteria with epidemic potential in the clinical studies on SARS-CoV-2;
4. To incorporate the validated SOPs in clinical trials and to follow-up on implementation by questionnaires;
5. To conduct external quality assessment to objectively assess the preparedness of laboratories;
6. To assist in finalization of the clinical protocol by adjusting SOPs, previously developed for the PREPARE clinical trials, in line with the study objectives for standardised and harmonised sampling, and to provide these sampling materials;
7. To perform exhaustive etiologic diagnosis on the samples collected from patients included in the clinical trials;
8. To correlate viral load at baseline in SARS-CoV-2 positive patients with severity of disease in Primary Care and hospitalised patients;
9. To expand the PREPARE Biobank with patient informed consent well-characterised clinical specimens from the prospective clinical trials for use in further studies.

### Description of work and role of partners

**WP4 - Lab support services** [Months: 1-24]

**UANTWERPEN, ERASMUS MC**

**Task 4.1: Select within PREPARE the laboratory facility to support the clinical networks (UA)**

Within the European laboratory facility LAB-Net, an established network of approximately 800 laboratories in 41 European countries to support clinical networks covering both Primary Care (PC) settings and Hospital Care (HC) settings, local laboratory infrastructures providing basic and or advanced diagnostic capacity to support the clinical trials on the SARS-CoV-2 will be identified. Most of these labs have been involved in previous PREPARE studies. To facilitate this site selection process, a feasibility questionnaire, developed in collaboration with EVD-LabNet (www.evd-labnet.eu), will be sent that aims to collect study-specific information e.g. on their in-house methods and possibilities to implement protocols and methods developed in this WP4.

**Task 4.2: Deployment of diagnostic capacity for SARS-CoV-2 across WP2 and WP3 trials (UA)**

The SARS-CoV-2 virus is genetically distinct from any of the previously recognized human and zoonotic coronaviruses, although highest similarity has been observed with that of the SARS coronavirus. As with any emerging disease outbreak, routine diagnostic platforms do not include testing for the novel virus, and full validation of commercial diagnostics typically lags behind. The laboratory partners in this consortium were the first to establish SARS-CoV-2 coronavirus virological diagnostics, provided as reference protocol on the WHO website for SARS-CoV-2 following rapid and collaborative validation, and provision of essential controls and specificity panels through the EVAg repository (Corman et al., 2020)(https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance). A survey across the EU reference centres for emerging viral diseases and for influenza, conducted in the week after publication of the first virological assay showed that almost all EU/EEA countries have assays operational, but that capacity would rapidly be limiting in case of further evolution of the outbreak, and there currently is no diagnostic capacity in most hospitals. Therefore, a key component of pandemic preparedness will be the deployment of diagnostic capacity across clinical centres involved in the proposed studies. During the evolution of a pandemic, viral drift or mutations conferring resistance will be monitored through WP5, and when necessary be used to update the diagnostic PCR protocols.

a) We will use the combined power of this WP, supplemented by collaborating major networks or initiatives such as EVAg (www.european-virus-archive.com), to develop and deploy detection assays with the sense of urgency needed for clinical service. Provisional contracts will be made with oligonucleotide suppliers. Protocols and nucleic acid
controls, and harmonised standards to facilitate comparison of Ct values among different quantitative PCR platforms
will be generated and made available to requesting entities inside the consortium. New insights from sequencing data or
fundamental virological work, will feed again into PCR protocols if needed which will be validated and made available
to requesting labs.

b) The use of second generation commercial PCRs, POCTs and syndromic multiplex formats/platforms to screen for
presence of the SARS-CoV-2 and other clinically related pathogens will be explored and assays will be validated by
counter-testing in a standard laboratory setting. These validations will be performed with biobanked samples described in
Task 4.8 from well-characterized patients included in previous EU-funded clinical studies in the context of GRACE and
PREPARE, with laboratory-confirmed infections with respiratory pathogens, including those that might cross react such as
the human coronaviruses, and with samples from a control population included in the same studies and available in
the biobank described above. These validation data will enable a more rapid and wider deployment of these commercial
tests for diagnosis of SARS-CoV-2 infections. For prioritisation, if needed, we will align with the WHO R&D blueprint
strategy for diagnostics (EMC contact).

Tasks 4.3: Development of SOPs for standardized and harmonised laboratory-based (in-house) detection of SARS-
CoV-2 (UA)

Based on the activities described in Tasks 4.2a and 4.2b and based on continuous evaluation and validation of novel
rapid diagnostic methods, WP4 will provide input to participating laboratories with advice on choices of primers-probes,
SOPs on QC/QA of primer batches, internal and positive controls and/or SOPs, both for sample preparation and for
PCR based detection method(s) and test(s) to be used for individual patient management as well as in the clinical trials.

Tasks 4.4: To conduct external quality assessment EQA (UA)

Through inter-laboratory collaborations with e.g. EVD-LabNet (www.evd-labnet.eu) and EVAg (www.european-virus-
archive.com), and in collaboration with independent International External Quality Assessment (EQA) / Proficiency
Testing (PT) organizations such as QCMD, an External Quality Assessment (EQA) will be set up by:
- Development of EQA proficiency panel(s) and SOPs to objectively assess the performance of laboratories, engaged
  in the clinical trials, to detect the SARS-CoV-2 and other pathogens of interest, relevant to the study.
- Sending out EQA panels to sites involved in clinical trials, the main objective of this EQA being to confirm that
  laboratory’s SOPs and IQC procedures are working adequately.

Task 4.5: To assist in finalization of the clinical protocol by developing SOPs for standardized and harmonised sampling
in line with the study objectives, and to provide these sampling materials. (UA)

To provide scientifically sound and comparable results in the RECOVER clinical studies across Europe, standardized
procedures for sampling as well as sample processing, storage and transfer of samples are needed. We have previously
demonstrated the importance of such standardization in observational studies and case-control cohorts in the context
of GRACE and PREPARE. Building on this experience and expertise, WP4 will support clinical protocol development
and study teams by:
- Developing sampling SOPs with details on the choice of samples and sampling collection time points that should be
  collected in line with the study objectives.
- Development of SOPs with detailed instructions on sample processing locally, storage and transfer of samples to
  the central laboratory.
- Preparation of study materials (i.e. sample kits and materials) to facilitate the sample collection, and processing and
  storage of samples to the local lab.
- Provide logistics of sending sample kits to sites and recalling samples from sites by organizing shipments, and
  protocols will be developed for shipment, packaging and transport for diagnostic specimens and infectious agents in
  accordance with international guidelines such as the International Air Transport Association regulations and the EU
dangerous goods directive.
- Organisation of shipments to collaborating laboratories responsible for activities in WP4 and WP5.

Task 4.6 Exhaustive etiologic diagnosis the samples collected from patients included in WP2 and WP3 (UA)

Exhaustive etiologic diagnosis will be performed on the samples collected from patients included in the SARS-CoV-2
clinical trials, using state-of-the-art PCR technology developed and/or validated through WP4 and through other EU-
funded projects such as GRACE, PREPARE, EVD-LabNet (www.evd-labnet.eu) and EVAg (www.european-virus-
archive.com). For longitudinally sampled patients, PCR based etiologic diagnosis will be complemented with the suite
of assays developed in WP5 for antibody profiling, transcriptome analysis, virus sequencing e.a.

Task 4.7 To correlate viral load in CoV positive patients with severity of disease in Primary care (UA)

We have previously shown in patients with viral respiratory infections included in the EU GRACE project that
disease severity is correlated with viral load. As we will perform exhaustive etiologic diagnosis in this WP4 with both
standardized samples and PCR based tests, we will be able to correlate viral load data with clinical data on outcome and severity of disease collected in WP2.

Task 4.8: To build a Biobank by storing and distributing well-characterised strains and clinical specimens from the prospective clinical trials (UA)

A biobank has already been established in the framework of PREPARE and GRACE. This biobank includes a repository of clinical reference specimens, required to evaluate newly developed syndrome based molecular diagnostic assays and for future fundamental work e.g. on pathogenesis and virus-host interactions, virus characterisation, immune response, transcriptomics. The biobank will be expanded in the context of RECOVER by the storage of well-characterized clinical samples collected prospectively in the RECOVER observational clinical studies. A policy will be agreed by the Consortium to mobilize or share the repository of stored clinical material from confirmed cases from the biobank in case they need to be transferred to other labs for further in-depth testing or to develop novel rapid diagnostic tests. The repository of reference specimens will be supplemented by formalised agreements with pathogen collection infrastructures at public health institutes including e.g. Institut Pasteur, France; EVAg and others.

Participation per Partner

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List of deliverables

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<th>Lead beneficiary</th>
<th>Type</th>
<th>Dissemination level</th>
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<td>D4.1</td>
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<td>1 - UANTWERPEN</td>
<td>Report</td>
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<td>1 - UANTWERPEN</td>
<td>Report</td>
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<td>D4.3</td>
<td>Report on results of counter validation</td>
<td>1 - UANTWERPEN</td>
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<td>D4.4</td>
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<td>D4.6</td>
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<td>Report</td>
<td>Public</td>
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Description of deliverables

D4.1 Feasibility questionnaire to collect information e.g. on in-house methods and possibilities to implement protocols and methods to detect the SARS-CoV-2
D4.2 Validation report on ready to use in-house PCR based test to be used in the clinical trial.
D4.3 Report on results of counter validation second generation commercial PCRs, POCTs and syndromic multiplex formats
D4.1: Feasibility questionnaire [3]
To facilitate the site selection process, a feasibility questionnaire will be sent that aims to collect study-specific information e.g. on in-house methods and possibilities to implement protocols and methods to detect SARS-CoV-2.

D4.2: Validation report on PCR based test [6]
Validation report on ready-to-use in-house PCR based test to be used in the clinical trial.

D4.3: Report on results of counter validation [18]
Report on results of counter validation second generation commercial PCRs, POCTs and syndromic multiplex formats.

D4.4: SOPs to standardise and harmonise diagnostic test protocols [4]
SOPs to standardise and harmonise diagnostic test protocols for detection of the SARS-CoV-2 and/or exclusion of other respiratory viral and bacterial pathogens.

This deliverable includes sampling SOPs with details on the choice of samples and sampling collection time points that should be collected in line with the study objectives and SOPs with detailed instructions on sample processing locally, storage and transfer of samples to the central laboratory.

D4.6: Results of etiologic diagnosis [24]
Results of etiologic diagnosis on the samples from patients included in the clinical trials on the SARS-CoV-2 in WP2 and WP3.

### Schedule of relevant Milestones

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<th>Milestone number</th>
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<th>Due Date (in months)</th>
<th>Means of verification</th>
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## Work package number

WP5

## Lead beneficiary

4 - ERASMUS MC

## Work package title

Clinical biology studies

## Start month

1

## End month

24

### Objectives

**WP5a Europe**

The overall goal is to provide answers to key outstanding questions on SARS-CoV-2 severity and transmissibility during evolution of the current epidemic and in the European context. This work will build on the expertise in MERS, SARS, and human coronaviruses, and refocus the tools developed for studies of these pathogens in PREPARE, COMPARE and ZAPI to include the SARS-CoV-2. We will adapt and employ multi-antigen serology, pathogen genomics and bioinformatics, host B-cell antibody profiling and transcriptome analysis. Biobanked samples and transcriptome data from well characterised patients infected with known human coronaviruses from PREPARE, and other networks (e.g. REACTing), as well as serum samples from experimentally infected or immunised animals will serve as a reference set, allowing rapid determination of common and unique markers for SARS-CoV-2 infection.

The research objectives of the patient-based lab studies are:

- To prepare essential protocols and standards for the laboratory evaluation of patient samples collected through the WP2, 3 and 6 studies
- To provide characterisation of viruses through in vitro and in vivo studies, to allow phenotypic characterisation of antigenic, virulence, and possible resistance traits for rapid risk assessment purposes
- To assess the possible role of prior coronavirus exposures to susceptibility, severity and transmissibility (EMC lead);
- To characterize the host transcriptome in patients with SARS-CoV-2 in order to understand development of severe disease and identify biomarkers for severity (AMC lead).

In addition, the following population-based study objectives will be addressed:

- To monitor evolution of the epidemic and contribute to the reference database for precision public health by characterization of viral genomes and phenotypic traits
- To determine the population incidence of cross-reactive antibodies in selected sites in Europe in liaison with the ECDC coordinated seroprevalence study.

**WP5b China-EU collaboration**

This work package is a collaboration between WP5 and the Pasteur Institute of Shanghai (member of the Institut Pasteur Asia Pacific Network) and the Chinese Academy of Science Affiliated Hospital in Hefei. The proposed research is aligned with the objectives listed in WP5. In case of successful funding, their partnership is eligible for matching funding from China through bilateral treaties with the EU and Ministry of Science and Technology of the People’s Republic of China (MOST). IP Shanghai provides the laboratory research support for the Chinese Academy of Science Affiliated Hospital in Hefei, which is a designated centre for the case of patients infected with SARS-CoV-2. Anhui province at present has 800 patients, and is expecting to see more given the local epidemiology at present, although stringent quarantine measures have been imposed, aiming to contain the spread of SARS-CoV-2.

The research objectives of the patient-based laboratory studies are:

- To describe the natural history of SARS-CoV-2 in relation to transmissibility in patients admitted to the Hefei hospital.
- To provide characterisation of viruses, to allow phenotypic characterisation and characterisation of immune response for rapid risk assessment purposes
- To assess the possible role of prior coronavirus exposures to susceptibility, severity and transmissibility;

In addition, the following population-based study objectives will be addressed:

- To monitor evolution of the epidemic and contribute to the reference database for precision public health by characterization of viral genomes and phenotypic traits

### Description of work and role of partners

**WP5 - Clinical biology studies** [Months: 1-24]

ERASMUS MC, UANTWERPEN, IP, CHARITE, AMC

Task 5.1 (month 1-24) To prepare essential protocols and standards for the laboratory evaluation of patient samples collected through the WP2, 3 and 6 studies (Charité)
Patients sampled according to the MERMAIDS or CCP protocol will be tested for virus shedding using calibrated quantitative RT-PCR assays to determine kinetics of shedding in diverse body compartments (upper, lower RT, stool, …), in relation to clinical presentation. The enhanced sampling studies will typically be done as part of national efforts, but this WP will provide reference laboratory support for those studies if needed. We will develop protocols for quantitative viral load monitoring, and prepare standards and protocols for harmonization of results from data generated in national reference laboratories across Europe. This will allow the pooling of individual patient data into the agreed global database. This includes development of protocols for post mortem immunopathological analyses in order to determine the tissue and cell tropism of SARS-CoV-2 in the respiratory tract. Assays ready for use will be transferred to WP4 for the observational studies.

Task 5.2 (month 1-24) To provide in depth characterisation of viruses through in vitro and in vivo studies, to allow phenotypic characterisation of antigenic, virulence, and possible resistance traits for rapid risk assessment purposes (Charité lead).

Unlike for influenza viruses, there is no agreed system for monitoring strain evolution, including genome changes that would trigger a deeper analysis of possible phenotypic changes that are relevant for detection, treatment or interventions. Based on fundamental knowledge on properties of SARS-CoV, we will develop an initial set of tools for assessment of essential properties that would potentially change public health risk and / or treatability. This will include indicator cell lines for transmembrane protease-based entry, infection assays on models of the human respiratory tract (air liquid interface culture) and replication therein, interferon and serum neutralization sensitivity, as well as genome surveillance and potential reconstruction of encountered mutants by reverse genetics. In conjunction with task 5.5, selected strains will be amplified by cell culture isolation and characterised for these phenotypic traits.

A key outstanding question is how transmissible is SARS-CoV-2, which is addressed through contact studies described in WP6. As part of the suit of reference systems for risk assessment, we will do a limited number of animal infection experiments using the expertise of the influenza virus transmissions studies at Erasmus MC to quantify transmissibility of SARS-CoV-2 compared to SARS. Samples from this study will be available for assay validation studies. The animal work will be combined with environmental sampling and in vitro studies to assess questions regarding virus stability and persistence. This information is important for development of evidence based guidelines for infection prevention.

Task 5.3 (month 1-24) To assess the possible role of prior coronavirus exposures to susceptibility, severity and transmissibility (EMC lead) Task 1.

We will develop antibody assays based on platforms used in the partner institutes (protein array, LIPS, pseudotype assays) targeting CoV spike (S1 and full length spike protein) and nucleoprotein (NP) representative for the diversity of seasonal human (HKU1, 229E, OC43 and NL63), and recent zoonotic (SARS and MERS). Antibody landscapes in individuals with known infections with key target CoVs will be compared. For this we will use well-defined longitudinal serum collections from RT-PCR confirmed humans obtained through collaboration with PREPARE and other networks (e.g. REACTing), and the virology diagnostic reference labs at the Erasmus MC, Charité and IP. The outcomes will be linked to functional assays, including antibody virus neutralization tests, to assess if these landscapes can be used to measure immune responses that correlate with severity of disease and transmissibility. For selected individuals we will generate B-cell profiles from peripheral blood mononuclear cells and immortalize specific B-cell clones that are representative for the antigenic breadth. These will be used to produce monoclonal antibodies (mAb) for validating specificity of protein and peptide arrays and as standard for other serological assays. Recombinant mAbs will be shared across labs via the EVAg platform.

Task 5.4 (month 1-24) To characterize the host transcriptome in patients with SARS-CoV-2 in order to understand development of severe disease and identify biomarkers (AMC lead).

In the PREPARE project, host transcriptomes were analysed of patients infected with a range of common respiratory pathogens, presenting in primary care or admitted to hospitals. Using these standardized analysis pipelines developed in PREPARE, genome-wide expression profiling will be done by microarray- and RNA seq-based methods in peripheral blood and nasopharyngeal specimens from patients with mild (primary care) and moderate to severe (hospitalized) SARS-CoV-2 infections, collected in observational studies of WP3. Gene expression profiles from SARS-CoV-2 infected patients will be analysed in the context of those from patients with other laboratory-confirmed acute respiratory infections, including human CoV infections (n=75), generated in the PREPARE MERMAIDS-ARI study. We will compare the transcriptome of patients with mild and severe SARS-CoV-2 infection, and analyse them comparatively for possible signatures associated with severity. In addition, the antibody landscapes for the patient groups included in this analysis will be compared.

Task 5.5 to monitor evolution of the epidemic and contribute to the reference database for precision public health (IP lead).
Viruses arising from recent spill over events may acquire changes when spreading in broader regions and populations. In case the outbreak evolves into a pandemic, systematic monitoring of the evolution of the viruses will be crucial to assess fit with diagnostic primers, monitor evolution of specific virus traits that could affect replication, treatability or antigenicity. Virus positive samples from the EU wide population snapshot collected through the GP network will be subjected to full genome sequencing to track the evolution for close to real-time phylodynamic and phylogeographic analysis. Selected viruses will be characterized in the risk analysis suite of assays developed in task 5.2. This data will be combined with classical epidemiological information to model transmission dynamics, identify genotype-phenotype associations and infer key epidemiological parameters.

For real-time monitoring of the evolution of the SARS-CoV-2 genome, (overlapping) amplicon-based sequencing will be performed using Minion. For low viral load samples, if needed, an enrichment approach specifically targeting SARS-CoV-2 or all betacoronaviruses will be used in order to be able to perform a more exhaustive search. This enrichment approach consists of designing probes that are specific to pre-selected coronavirus genomes and using them to specifically capture the DNA fragments corresponding to the viral genomes and sequence them either by a 2nd generation sequencer (HiSeq for example) or by using real-time nanopore sequencing technology. The SARS-CoV-2 sequences obtained by these different approaches will be analysed in order to better understand the evolution of this virus and its transmission.

Task 5B.1 (month 1-24) To describe the natural history of SARS-CoV-2 in relation to transmissibility in patients admitted to the Hefei hospital

In the Chinese Academy of Science Affiliated Hospital in Hefei, after positive diagnostic, we are enrolling patients after obtaining their consent to obtain samples. Patients sampled will be tested for virus shedding using calibrated quantitative RT-PCR assays to determine kinetics of shedding in diverse body compartments (upper, lower RT, stool, …), in relation to clinical presentation. The enhanced sampling studies will be done as part of a local study. When possible, data will be bridged with data collected in the EU studies by use of agreed standards and validation panels provided by partners in Europe. This will allow the pooling of individual patient data into the agreed global database if cleared by the national authorities.

Task 5B.2 (month 1-24) To provide in depth characterisation of viruses through in vitro and in vivo studies, to allow phenotypic characterisation of antigenic, virulence, and possible resistance traits for rapid risk assessment purposes

Using samples from patients, virus strains will be amplified by cell culture isolation. Genome will be sequenced (see Task 5.5). Unlike for influenza viruses, there is no agreed system for monitoring strain evolution, including genome changes that would trigger a deeper analysis of possible phenotypic changes that are relevant for detection, treatment or interventions. We will do characterization using growth curve and we will implement some relevant assays developed and validated by EU partners (see WP5 Task 5.2).

The collaborating institutes in China have developed a shared platform for sequencing analysis. Relevant observations will be shared for the Task 5.2 studies in the EU WP 5.

Task 5B.3 (month 1-24) To assess the possible role of prior coronavirus exposures to susceptibility, severity and transmissibility

We will develop antibody assays targeting CoV spike (S1 and full length spike protein), RBD and nucleoprotein (NP) representative for the SARS-CoV-2, SARS and MERS, and measure antibody kinetics in patients from the outbreak. We will conduct neutralization assays using viruses isolated from the same patient, but also reference strain from SARS-CoV-2 and SARS CoV. These neutralization titres and the antigen- specific binding antibody responses will allow better understanding how humans respond to this virus and may potentially identify key epitopes.. Assays developed in the EU funded project that can be implemented locally (i.e. protein array) will be included for comparative analysis, as part of the need for standardisation of serological assays.

We will develop SARS-CoV-2 high-efficiency human-neutralizing antibodies. Two strategies will be used. The first is to modify the SARS-based neutralizing monoclonal antibodies. Two potent SARS neutralizing antibodies have been chosen based on the structure and bioinformatics-based mutants are being designed and expressed as recombinant humanized monoclonal antibodies. The second strategy is to clone and express monoclonal antibodies from single B cells of convalescent patients. SARS-CoV-2 Spike S or S1-RBD protein will be labelled with fluorescence dyes which
is used to capture antigen-specific B cells. Single B cell is sorted and the heavy and light chains of BCR are cloned and expressed. All Candidate antibodies will be tested for neutralizing capacities by using pseudoviral system in P2 and SARS-CoV-2 cell culture system in BSL3 labs. The potential of cross neutralisation against different SARS-CoV-2 patient isolates and SARS CoV strains will be evaluated. The best candidates will be test in animals and they can be include in transmission animal studies develop by EU partners.

Task 5B.4 (month 1-24) To characterize the possible relevance of CD4 lymphopenia in pathogenesis Using SARS-CoV-2 patients cohorts and permissive animal models we will determine the functional correlation of reduction of CD4 T cell counts and soluble CD4 protein with the severity of CoVID-19. We will define activation of macrophages/NK cell and how they trigger thymic evolution and reduced T cell migration or and CD4 T cell death in the periphery. Using mice model, we will establish therapeutic efficacy of recombinant CD4 in suppression hyperactivated systemic inflammation of SARS-CoV-2 mice. In parallel to antibody response, the longitudinal study of innate and adaptive responses in patients will allow better understanding how humans respond to this virus and may potentially identify a sero-biomarker associated with viral clearance or patient recovery. These results will be compared

Task 5B.5 To monitor evolution of the epidemic and contribute to the reference database for precision public health Viruses arising from recent spill over events may acquire changes when spreading in broader regions and populations. In case the outbreak evolves into a pandemic, systematic monitoring of the evolution of the viruses will be crucial to assess fit with diagnostic primers, monitor evolution of specific virus traits that could affect replication, treatability or antigenicity. IP Shanghai developed a secure shared platform for strain evolution monitoring, which allows data submission portal used by clinical labs and hospital staff, functional modules for real time epidemic tracking and reporting with algorithms for virus evolution and population modelling, and a reporting module for end users’ feedback and warning of relevant agency. Shanghai city and Guangdong province have submitted samples data to the platform. The functioning of this platform will be compared with other models for data sharing, as developed through COMPARE, GISRS, and the open data models. A joint report will assess approaches and barriers to rapid sharing of essential data.

For real-time monitoring of the evolution of the SARS-CoV-2 genome, (overlapping) amplicon-based sequencing will be performed using Minion. For low viral load samples, if needed, an enrichment approach specifically targeting SARS-CoV-2 or all betacoronaviruses will be used in order to be able to perform a more exhaustive search, and protocols will be exchanged between the collaborating partners. This enrichment approach consists of designing probes that are specific to pre-selected coronavirus genomes and using them to specifically capture the DNA fragments corresponding to the viral genomes and sequence them either by a 2nd generation sequencer (HiSeq for example) or by using real-time nanopore sequencing technology. The SARS-CoV-2 sequences obtained by these different approaches will be analysed in order to better understand the evolution of this virus and its transmission. The possible use of genomic sequencing for cluster analysis will be explored, following initial results based on a familial cluster case reported from Guangdong, suggesting single origin of this family cases and probably viral evolution occurred after human to human transmission. More in depth analysis will be done using NGS.

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<td>Transmissibility report</td>
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<td>Report on real-time viral tracking</td>
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### Description of deliverables

Deliverable due dates are given, but in line with the current policy during the PHEIC, any findings that may be relevant for the wider community involved in epidemic response will be shared through WHO.

D5.1. Report summarizing first generation methods for characterisation of SARS-CoV-2 for rapid risk assessment, essential infection dynamics to inform hospital infection prevention guidelines (Month 24)

D5.2 Report describing transmissibility of SARS-CoV-2 in comparison with SARS in an animal model (Month 6)

D5.3 First validated serological assay (Month 6)

D5.4 Report on specific and cross reactive antibodies to coronaviruses (Month 12)

D5.5 Biomarkers for SARS-COV-2 infection (Month 24)

D5.6 Joint EU-IP Shanghai report on approaches and barriers to real-time viral tracking (Month 24)

D5.7. Report on standardized seroincidence study (Month 24)

D5B.1 Essential infection dynamics to inform prevention guidelines (Month 24)

D5B.2 Report describing evolution of SARS-CoV-2 during a widespread outbreak in China (Month 6)

D5B.3 Report on specific and cross reactive antibodies to coronaviruses (Month 12)

D5B.4 Biomarkers for SARS-CoV-2 infection (Month 24)

D5B.5 Joint EU-IP Shanghai report on approaches and barriers to real-time viral tracking (Month 24)


Report summarizing first generation methods for characterisation of SARS-CoV-2 for rapid risk assessment, essential infection dynamics to inform hospital infection prevention guidelines

D5.2 : Transmissibility report [6]

Report describing transmissibility of SARS-CoV-2 in comparison with SARS in an animal model.

D5.3 : First validated serological assay [6]

First validated serological assay

D5.4 : Report on antibodies to COV [12]

Report on specific and cross reactive antibodies to coronaviruses.

D5.5 : Biomarkers for SARS-COV-2 infection [24]

Biomarkers for SARS-CoV-2 infection.

D5.6 : Report on real-time viral tracking [24]

Joint EU-IP Shanghai report on approaches and barriers to real-time viral tracking.

D5.7 : Report on standardized seroincidence study [24]

Report on standardized seroincidence study.
D5.8 : Essential infection dynamics [24]
Essential infection dynamics to inform prevention guidelines.
D5.9 : Report on outbreak evolution in China [24]
Report describing evolution of SARS-CoV-2 during a widespread outbreak in China.
D5.10 : Report on antibodies to COV (IPS) [24]
Report on specific and cross reactive antibodies to coronaviruses.
D5.11 : Biomarkers for SARS-CoV-2 infection (IPS) [24]
Biomarkers for SARS-CoV-2 infection.
D5.12 : Report on real-time viral tracking (IPS) [24]
Joint EU-IP Shanghai report on approaches and barriers to real-time viral tracking.

Schedule of relevant Milestones

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**WP6 - Transmission, epidemic dynamics and modelling [Months: 1-24]**

**INSERM, IP, UMC UTRrecht**

Task 6.1 Studying the risk of SARS-CoV-2 infection in contacts of confirmed cases (INSERM, months 1-12)

The contact study, which has already been launched in France and will be shared with other countries to ensure standardization of the method across Europe, will be conducted among moderate/high-risk contacts of confirmed SARS-CoV-2 cases, the latter having been identified in the clinical studies in primary or secondary care described in WP2 and WP3. At selected sites, moderate/high-risk contacts will be joined by a practitioner (or his delegate) to inform them of the study and to obtain oral consent. As moderate/high-risk contacts are currently isolated during 14 days according to the incubation phase estimations, they cannot exit from their home. Consequently, a study nurse will visit them at home, collect the signed informed consent, take a blood sample and perform a nasal and/or throat swab as soon as possible after the moderate/high-risk contacts have been identified. Using dedicated video, nurses will teach contacts how to self-collect nasal swabs at days 3, 5, 7 and 13 after the last identified moderate/high-risk contacts with the confirmed SARS-CoV-2 cases. Early in the epidemic, samples will not be allowed to be sent by mail. At this stage, the nasal samples packed according to the country's legislation will therefore be transported in ambient air by a dedicated courier to the virology lab of the reference medical centre and specific SARS-CoV-2 RT-PCR performed as soon as possible. These samples will be sent by mail as soon as this will be allowed by regulations. A self-administered questionnaire will be filled-out by the contact twice daily during 14 days, recording temperature and flu-like symptoms on a semi-quantitative scale using a modified version of an interactive diary application that was previously used in a study among healthcare workers on respiratory infections. Upon occurrence of relevant symptoms, the app will send out a notification to the practitioner in charge of this protocol or his delegate. The practitioner will coordinate with the general practitioner to manage the patients' health according to the current country policy. If the patient were to become infected with the coronavirus, he/she would be managed within the framework of WP2 or WP3. In the event of systematic SARS-CoV-2 RT-PCR positivity, the contacts will be taken care of as a SARS-CoV-2 infected patient. In all individuals, a second blood sample will be taken at day 90 for serology. This protocol may be extended to other individuals with high risk of exposure to SARS-Cov-2.

Task 6.2 Studying household transmission of SARS-CoV-2 (UMCU – months 2-14)

Once sustained local transmission of SARS-CoV-2 has been established, it is important to characterize the population dynamics of transmission. Transmission within households is a key process driving the epidemic of many respiratory viruses such as influenza and RSV. Household studies are therefore a useful approach to obtain insight into the main determinants of transmission and to derive estimates of transmission parameters. By fully characterizing the critical process of SARS-CoV-2 household transmission, infection dynamics in the population can be further elucidated. The household study will be conducted among household members of confirmed SARS-CoV-2 index patients that are identified in the clinical studies in primary or hospital care described in WP2 and WP3, at sites where sustained local transmission of SARS-CoV-2 has been confirmed and that have been pre-selected for the household study. At these sites, study nurses will approach patients and their household members for participation in the household study. Stratified enrollment will be applied to assure the household cohort covers a range of household sizes and age-groups. Households should have a minimum size of two, no other symptomatic individual in the household upon enrollment and can participate when consent is obtained for all household members. If households respond favorably to the invitation, a study home visit is planned for informed consent, to teach household members of age how to collect a nasal flocked swab and perform nasal swabs at days 7, 13, 21, 28 and 56 after the last identified moderate/high-risk contacts with the confirmed SARS-CoV-2 cases. Early in the epidemic, samples will not be allowed to be sent by mail. At this stage, the nasal samples packed according to the country's legislation will therefore be transported in ambient air by a dedicated courier to the virology lab of the reference medical centre and specific SARS-CoV-2 RT-PCR performed as soon as possible. These samples will be sent by mail as soon as this will be allowed by regulations. A self-administered questionnaire will be filled-out by the contact twice daily during 14 days, recording temperature and flu-like symptoms on a semi-quantitative scale using a modified version of an interactive diary application that was previously used in a study among healthcare workers on respiratory infections. Upon occurrence of relevant symptoms, the app will send out a notification to the practitioner in charge of this protocol or his delegate. The practitioner will coordinate with the general practitioner to manage the patients’ health according to the current country policy. If the patient were to become infected with the coronavirus, he/she would be managed within the framework of WP2 or WP3. In the event of systematic SARS-CoV-2 RT-PCR positivity, the contacts will be taken care of as a SARS-CoV-2 infected patient. In all individuals, a second blood sample will be taken at day 90 for serology. This protocol may be extended to other individuals with high risk of exposure to SARS-Cov-2.
swab and a throat swab specimen and have participants collect the first specimen under direct observation by research staff, and to complete a baseline questionnaire detailing family characteristics and medical history. Household members will be asked to collect nasal and throat swabs on the 1st or 2nd day of new onset respiratory symptoms, or at least weekly when no symptoms occur. Samples are mailed to the study laboratory for viral PCR. Past studies have shown that self-collection of swabs feasible, efficient, and acceptable by study participants, and does not significantly reduce detection rates (29–31). All nasal and throat swabs will be screened for respiratory viruses (32), including SARS-CoV-2, other human coronaviruses, and other major respiratory viruses such as RSV (A and B), Influenza virus (A and B), PIV (1-3), hMPV, and human rhinovirus. Household members will also be asked to record ARI symptoms on a daily basis, including severity of the symptoms and whether they sought medical care. For this, we capitalize on our expertise in monitoring community infections by means of an interactive diary App. In our previous studies, this technique achieved 95–97% data completeness, 85% sample collection, and high discrimination of disease severity (33–35).

Task 6.3 Estimation of parameters characterizing SARS-CoV-2 transmission in Europe and of the impact of existing control interventions (IP, INSERM – months 1-16)
From the detailed studies documenting SARS-CoV-2 infections in contacts of European cases (Tasks 6.1-6.2) as well as patient excretion data (WP5), we will estimate key transmission parameters of SARS-CoV-2 in Europe, including the transmission rate, the incubation period, the generation time, the proportion of transmissions that occur prior to symptom onset, the susceptibility and infectiousness of different types of individuals (e.g. children vs adults) and the risk of super-spreading events. A major challenge to estimate these parameters from such data is that the transmission process is imperfectly observed. For example, it may be impossible to determine who was infected by whom in a cluster of cases; times of exposure may be imperfectly characterised; transmission will be censored by the implementation of control interventions. We will develop a mathematical model to characterize SARS-CoV-2 person-to-person transmission and use well-established data augmentation Bayesian techniques to address the missing data issues mentioned above and reliably estimate transmission parameters.7 The statistical framework will also make it possible to evaluate the proportion of transmissions avoided thanks to existing containment interventions. We will also model intra-host viral dynamics from patient excretion data collected in WP5 to estimate from these data key parameters characterizing viral dynamics (virus infectivity, half-life of infected cells, impact of innate immunity on viral control and pathogenicity)8.

Task 6.4 Evaluation of the impact of possible social distancing measures on SARS-CoV-2 spread (INSERM, IP – Months 4-16)
Once transmission parameters have been estimated (Task 6.3), they will be integrated in a meta-population model that will be used to simulate realistic SARS-CoV-2 epidemic under different control scenarios. The model is data-driven and spatially structured at municipality level. Mixing is modeled with a contact matrix based on two age classes (children/adults) and informed with available data on contacts established at different locations (e.g. home, workplace, school) and how they change in time (e.g. weekday vs. weekend, school term vs. school holiday). Coupling between municipalities is modeled through age-specific commuting data, and air travel data. The model has already been used to evaluate the impact of school closure and validated on seasonal flu. A number of different interventions will be considered for example school and workplace closures, work-at-home recommendation, quarantines of areas, cancellation of mass gatherings.

Task 6.5 Continued monitoring of the risk of importation of SARS-CoV-2 in Europe (INSERM, Months 1-4)
We have developed a model to characterize the European risk of importation of SARS-CoV-2 from China9. As the situation quickly evolves internationally, this model will be regularly revised to monitor the risk of importation. In particular, we will estimate the amplified risk for Europe in the scenario of SARS-CoV-2 epidemic being established in Africa following importation from China. We already estimated the risk for African countries to import a case and assessed their capacity to respond, based on air travel flows from China and accounting for incidence levels in the affected Chinese provinces, as well as travel restrictions in Wuhan. A set of African countries were found to be at moderate risk that have large population sizes, varying functional capacity and high vulnerability to infectious disease threats. This task will evaluate the shift in the risk for Europe if an epidemic becomes sustained in one of these countries.

Task 6.6 Monitoring behavior changes through participative surveillance platforms (INSERM, months 1-6)
The Task will collect data on knowledge, perceptions, fears, attitudes and behaviors with respect to the SARS-CoV-2 epidemic. This will be done through the participative platform GrippeNet.fr, developed by Inserm and Sante publique France since 2011 to monitor influenza-like-illness and associated behaviors. The platform now counts approximately 6,000 participants resident in France who respond weekly to a set of questions around influenza-like-illness and associated behaviors (e.g. health-seeking behavior, vaccination, drugs uptake). We plan to add 2 layers of questions: 1) A survey to measure knowledge, perceptions, fears towards SARS-CoV-2 epidemic that may drive specific attitudes. This will be sent at different phases of the epidemic, during sporadic importation, chains of transmission, established epidemic. 2) Additional questions to be asked within the weekly survey on symptoms to (2.1) enlarge the case definition and add history of travel; and to (2.2) measure change of behaviors (e.g. avoiding restaurants, crowded
places, increasing telework, etc.) that may alter the course of the epidemic. GrippeNet.fr is part of a European network of participative surveillance (InfluenzaNet) including 11 countries. The surveys will be translated in the different languages and integrated in the other platforms to collect a vast set of data across different countries.

The following tasks will be implemented in phase II:

Task 6.7 Nowcasting and forecasting to inform planning activities (IP, INSERM)
If the epidemic becomes widespread, monitoring its local trajectory will become essential to inform planning activities. Such monitoring may however be challenging since a number of other respiratory viruses will be circulating at the same time and health seeking behaviours may be strongly modified because of concerns in the population. We will develop a Bayesian statistical framework to nowcast the epidemic from the integration of multiple data streams collected within this consortium on primary care (WP2) and hospitalisation data (WP3), serosurveys (WP5), behavioural studies (Task 6.6) but also from national syndromic and virological surveillance. We will also use a suit of mathematical models to forecast the epidemic trajectory in European countries to inform planning activities. A subset of these models will be spatially explicit and integrate mobility data, from commuting to air travel. Thanks to the detailed data collected in WP3 documenting the trajectory of patients in hospital, we will be able to forecast needs in terms of hospital capacity.

Task 6.8 Long-term patterns of circulation and implications for Public Health (IP INSERM)
If the epidemic is not quickly contained, a major question for Public Health will be to determine what the expected long-term patterns of circulation of SARS-CoV-2 and implications for control. For example, will circulation get extinct after a first pandemic wave? If it does persist, what will be the expected frequency of epidemics, attack rate, disease burden? Which vaccinations strategies should be considered either to mitigate local epidemics or to eradicate the disease? Mathematical models describing the spread of SARS-CoV-2 at different scales (worldwide vs national) and in different populations (by age group and comorbidities) will be constructed to investigate these questions.

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### Description of deliverables

D6.1 First batch of contact data available for modelling - Month 1  
D6.2 First batch of household data available for modelling (one month after the start of widespread transmission)  
D6.3 Early estimates of transmission parameters - Month 4  
D6.4 Early evaluation of the impact of social distancing measures - Month 4  
D6.5 First estimates of the perceptions about SARS-CoV-2 and of health-seeking behaviours - Month 2  
D6.6 Availability of real-time monitoring of the risks of importation of SARS-CoV-2 in Europe - Month 1  
D6.7 Nowcasting and forecasting of an epidemic (one month after the start of widespread transmission in Europe)  
D6.8 Evaluation of the long-term implications for Public Health - Month 16

D6.1 : Contact data available for modelling [3]  
First batch of contact data available for modelling.  
First batch of household data available for modelling (one month after the start of widespread transmission).  
Early estimates of transmission parameters.  
D6.4 : Evaluation of social distancing measures [4]  
Early evaluation of the impact of social distancing measures.
D6.5 : First estimates of perceptions
First estimates of the perceptions about SARS-CoV-2 and of health-seeking behaviours.

D6.6 : Real-time monitoring of risks
Availability of real-time monitoring of the risks of importation of SARS-CoV-2 in Europe.

D6.7 : Nowcasting and forecasting of an epidemic
Nowcasting and forecasting of an epidemic (one month after the start of widespread transmission in Europe).

D6.8 : Implications for public health
Evaluation of the long-term implications for public health.

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Schedule of relevant Milestones

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**Work package number**  WP7  **Lead beneficiary**  1 - UANTWERPEN

**Work package title**  Ethics requirements

**Start month**  1  **End month**  24

### Objectives

The objective is to ensure compliance with the 'ethics requirements' set out in this work package.

### Description of work and role of partners

**WP7 - Ethics requirements**  [Months: 1-24]

**UANTWERPEN**

This work package sets out the 'ethics requirements' that the project must comply with.

### List of deliverables

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<td>H - Requirement No. 14</td>
<td>1 - UANTWERPEN</td>
<td>Ethics</td>
<td>Confidential, only for members of the consortium (including the Commission Services)</td>
<td>3</td>
</tr>
</tbody>
</table>

### Description of deliverables

The 'ethics requirements' that the project must comply with are included as deliverables in this work package.

**D7.1 : H - Requirement No. 2 [3]**

1. The procedures and criteria that will be used to identify/recruit research participants must be must be submitted as a deliverable. 2. The informed consent/assent procedures of children and adults unable to give informed consent involved in the research and details on how the consent of the legal representatives will be acquired must be submitted as a deliverable. 3. In case vulnerable individuals/groups are involved in the study, details must be submitted as deliverable about the measures taken to prevent the risk of enhancing vulnerability/stigmatisation of individuals/groups.

**D7.2 : H - Requirement No. 3 [12]**

1. Templates of the informed consent/assent forms and information sheets (in language and terms intelligible to the participants) must be kept on file and made available to the EC upon request. 2. Copies of opinions/approvals by ethics committees and/or competent authorities for the research with humans must be submitted as a deliverable. 3. For each clinical study, the following documents/information must be submitted as a deliverable (in one package) prior to enrolment of first study subject: (i) Final version of study protocol as submitted to regulators/ethics committee(s), (ii) Registration number of clinical study in a WHO-or ICMJE- approved registry (with the possibility
to post results), (iii) Approvals (ethics committees and national competent authority if applicable) required for invitation/enrolment of first subject in at least one clinical centre.

D7.3 : H - Requirement No. 4 [24]
1. For each clinical study, a report on the status of posting results in the study registry(s) must be submitted as a deliverable, including timelines if/when final posting of results is scheduled after end of funding period.

D7.4 : HCT - Requirement No. 5 [6]
1. In case human cells/tissues are obtained within the project, details on cells/tissues type must be provided. The beneficiary must also confirm that relevant approvals have been obtained and is kept on file. 2. In case human cells/tissues are obtained within another project/institution, details on cells/tissues type must be provided. The beneficiary must confirm that authorisation has been obtained from the primary owner of cells/tissues (including references to ethics approval) and is kept on file. 3. Copies of relevant documents for using, producing or collecting human cells (i.e. ethics approval, accreditation/designation/authorisation/licensing) must be submitted as a deliverable.

D7.5 : POPD - Requirement No. 7 [3]
1. The applicants must confirm that a Data Protection Officer (DPO) has been appointed and that the contact details of the DPO are made available to all data subjects involved in the research. For host institutions not required to appoint a DPO under the GDPR a detailed data protection policy for the project must be submitted as a deliverable. 2. A description of the technical and organizational measures that will be implemented to safeguard the rights and freedoms of the data subjects/research participants must be submitted as a deliverable. 3. Detailed information on the informed consent procedures in regard to data processing must be submitted as a deliverable. 4. Templates of the informed consent forms and information sheets must be submitted as a deliverable. 5. A description of the security measures that will be implemented to prevent unauthorized access to personal data or the equipment used for processing must be submitted as a deliverable.

D7.6 : A - Requirement No. 8 [3]
1. Details regarding the animal (mouse and ferrets) studies, including enrichment, 3R principles and human endpoints must be submitted as a deliverable.

D7.7 : A - Requirement No. 9 [12]
1. Copies of relevant authorisations for animal experiments (covering also the work with mice and genetically modified animals, if applicable) must be submitted as a deliverable. 2. Copies of training certificates/personal licenses of the staff involved in animal experiments must be kept on file and made available to the EC upon request.

D7.8 : EPQ - Requirement No. 11 [6]
1. The applicant must confirm that appropriate health and safety procedures conforming to relevant local/national guidelines/legislation are followed for staff involved in this project. This must be submitted as a deliverable. 2. Copies of authorisations for relevant facilities (i.e. security classification of laboratory) must be kept on file and made available to the EC upon request.

D7.9 : GEN - Requirement No. 12 [3]
1. An independent Ethics Advisor must be appointed to monitor the ethics issues involved in this project and how they are handled. The Advisor must be consulted among other issues on the following points: humans, data protection, animals, third countries, environment and human tissues.

D7.10 : GEN - Requirement No. 13 [12]
1. A report by the Independent Ethics Advisor must be submitted as a deliverable at the end of each reporting period.

D7.11 : POPD - Requirement No. 6 [3]
1. The beneficiary must explain how all of the data they intend to process is relevant and limited to the purposes of the research project (in accordance with the ‘data minimisation’ principle). This must be submitted as a deliverable. 2. Description of the anonymisation/pseudonymisation techniques that will be implemented must be submitted as a deliverable. 3. A description of the security measures that will be implemented to prevent unauthorised access to personal data or the equipment used for processing must be submitted as a deliverable.

1. Details on incidental findings policy must be submitted as a deliverable.
<table>
<thead>
<tr>
<th>Milestone number</th>
<th>Milestone title</th>
<th>Lead beneficiary</th>
<th>Due Date (in months)</th>
<th>Means of verification</th>
</tr>
</thead>
</table>

18

Associated with document Ref. Ares(2020)1861087 - 31/03/2020
### 1.3.4. WT4 List of milestones

<table>
<thead>
<tr>
<th>Milestone number</th>
<th>Milestone title</th>
<th>WP number</th>
<th>Lead beneficiary</th>
<th>Due Date (in months)</th>
<th>Means of verification</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS1</td>
<td>Phase I hospital study (MERMAIDS-ARI) initiated</td>
<td>WP3</td>
<td>5 - UOXF</td>
<td>1</td>
<td>Initiation of MERMAIDS-ARI hospital study</td>
</tr>
<tr>
<td>MS2</td>
<td>Protocol phase II completed</td>
<td>WP3</td>
<td>3 - UMC UTRECHT</td>
<td>2</td>
<td>Protocol Phase II MERMAIDS-ARI 2.0 completed</td>
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<tr>
<td>MS3</td>
<td>Phase II study sites selected</td>
<td>WP3</td>
<td>3 - UMC UTRECHT</td>
<td>2</td>
<td>New study sites for Phase II study selected</td>
</tr>
<tr>
<td>MS4</td>
<td>Approved protocol enhanced PPAS</td>
<td>WP2</td>
<td>5 - UOXF</td>
<td>2</td>
<td>Sponsor approved protocol for the observational study (enhanced PPAS) in Primary Care</td>
</tr>
<tr>
<td>MS5</td>
<td>Approvals in EU countries, green light for patient inclusions</td>
<td>WP2</td>
<td>5 - UOXF</td>
<td>6</td>
<td>Approvals in up to 20 EU and associated countries, green-light for patient inclusion.</td>
</tr>
<tr>
<td>MS6</td>
<td>Approved protocol adapted PRUDENCE trial</td>
<td>WP2</td>
<td>5 - UOXF</td>
<td>6</td>
<td>UK approved protocol for the adapted PRUDENCE trial for WP2.</td>
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<tr>
<td>MS7</td>
<td>Established procedures for sample storage and shipment</td>
<td>WP2</td>
<td>5 - UOXF</td>
<td>6</td>
<td>Contracts with local laboratories and established procedures for sampling, storing, sending samples to central laboratory.</td>
</tr>
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### 1.3.5. WT5 Critical Implementation risks and mitigation actions

<table>
<thead>
<tr>
<th>Risk number</th>
<th>Description of risk</th>
<th>WP Number</th>
<th>Proposed risk-mitigation measures</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Lengthy site contracting processes</td>
<td>WP1, WP2, WP3, WP4, WP5, WP6</td>
<td>Quick roll out of already active sites and networks in PREPARE</td>
</tr>
<tr>
<td>2</td>
<td>Lengthy IRB approval processes</td>
<td>WP1, WP2, WP3, WP4, WP6</td>
<td>Quick roll out of already active sites and networks in PREPARE</td>
</tr>
<tr>
<td>3</td>
<td>Clinical sites overwhelmed by SARS-CoV-2 epidemic in Europe</td>
<td>WP1, WP2, WP3, WP4, WP5, WP6</td>
<td>In this widespread circulation scenario, we expect to have a large number of sites participating in the studies, allowing us to gather sufficient data and samples even with low patient/samples inclusions per site.</td>
</tr>
</tbody>
</table>
1.3.6. WT6 Summary of project effort in person-months

<table>
<thead>
<tr>
<th>WP1</th>
<th>WP2</th>
<th>WP3</th>
<th>WP4</th>
<th>WP5</th>
<th>WP6</th>
<th>WP7</th>
<th>Total Person/Months per Participant</th>
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<td>- UZA</td>
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<td>0</td>
<td>0</td>
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<td>3 - UMC UTRECHT</td>
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<td>0</td>
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<td>4 - ERASMUS MC</td>
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<td>6 - CHARITE</td>
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<tr>
<td>Total Person/Months</td>
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<td>70</td>
<td>31.80</td>
<td>92.30</td>
<td>59.40</td>
<td></td>
</tr>
</tbody>
</table>
1.3.7. WT7 Tentative schedule of project reviews

No project reviews indicated
1. Project number

The project number has been assigned by the Commission as the unique identifier for your project. It cannot be changed. The project number should appear on each page of the grant agreement preparation documents (part A and part B) to prevent errors during its handling.

2. Project acronym

Use the project acronym as given in the submitted proposal. It can generally not be changed. The same acronym should appear on each page of the grant agreement preparation documents (part A and part B) to prevent errors during its handling.

3. Project title

Use the title (preferably no longer than 200 characters) as indicated in the submitted proposal. Minor corrections are possible if agreed during the preparation of the grant agreement.

4. Starting date

Unless a specific (fixed) starting date is duly justified and agreed upon during the preparation of the Grant Agreement, the project will start on the first day of the month following the entry into force of the Grant Agreement (NB: entry into force = signature by the Commission). Please note that if a fixed starting date is used, you will be required to provide a written justification.

5. Duration

Insert the duration of the project in full months.

6. Call (part) identifier

The Call (part) identifier is the reference number given in the call or part of the call you were addressing, as indicated in the publication of the call in the Official Journal of the European Union. You have to use the identifier given by the Commission in the letter inviting to prepare the grant agreement.

7. Abstract

8. Project Entry Month

The month at which the participant joined the consortium, month 1 marking the start date of the project, and all other start dates being relative to this start date.

9. Work Package number

Work package number: WP1, WP2, WP3, ..., WPn

10. Lead beneficiary

This must be one of the beneficiaries in the grant (not a third party) - Number of the beneficiary leading the work in this work package

11. Person-months per work package

The total number of person-months allocated to each work package.

12. Start month

Relative start date for the work in the specific work packages, month 1 marking the start date of the project, and all other start dates being relative to this start date.

13. End month

Relative end date, month 1 marking the start date of the project, and all end dates being relative to this start date.

14. Deliverable number

Deliverable numbers: D1 - Dn

15. Type

Please indicate the type of the deliverable using one of the following codes:

- R Document, report
- DEM Demonstrator, pilot, prototype
- DEC Websites, patent fillings, videos, etc.
- OTHER
- ETHICS Ethics requirement
- ORDP Open Research Data Pilot
- DATA data sets, microdata, etc.
16. Dissemination level

Please indicate the dissemination level using one of the following codes:

- **PU** Public
- **CO** Confidential, only for members of the consortium (including the Commission Services)
- **EU-RES** Classified Information: RESTREINT UE (Commission Decision 2005/444/EC)
- **EU-CON** Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC)
- **EU-SEC** Classified Information: SECRET UE (Commission Decision 2005/444/EC)

17. Delivery date for Deliverable

Month in which the deliverables will be available, month 1 marking the start date of the project, and all delivery dates being relative to this start date.

18. Milestone number

Milestone number: MS1, MS2, ..., MSn

19. Review number

Review number: RV1, RV2, ..., RVn

20. Installation Number

Number progressively the installations of a same infrastructure. An installation is a part of an infrastructure that could be used independently from the rest.

21. Installation country

Code of the country where the installation is located or IO if the access provider (the beneficiary or linked third party) is an international organization, an ERIC or a similar legal entity.

22. Type of access

- **VA** if virtual access,
- **TA-uc** if trans-national access with access costs declared on the basis of unit cost,
- **TA-ac** if trans-national access with access costs declared as actual costs, and
- **TA-cb** if trans-national access with access costs declared as a combination of actual costs and costs on the basis of unit cost.

23. Access costs

Cost of the access provided under the project. For virtual access fill only the second column. For trans-national access fill one of the two columns or both according to the way access costs are declared. Trans-national access costs on the basis of unit cost will result from the unit cost by the quantity of access to be provided.
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1. EXCELLENCE

1.1 Objectives

RECOVER (Rapid European SARS-CoV-2 Emergency Research response) originates from partners of the EU Framework 7 (FP7) funded PREPARE project (Platform for European Preparedness Against (Re-) emerging Epidemics, see www.prepare-europe.eu). This RECOVER application outlines PREPARE’s research response plan as part of its Mode 3 research response (see textbox below) to the SARS-CoV-2 epidemic. As the SARS-CoV-2 epidemic unfolds, we will adapt and redirect the RECOVER response research and budget to where it is considered most impactful, in close consultation with the EC and other stakeholders.

About PREPARE’s Outbreak Research Modes

PREPARE distinguishes three modes in its research response efforts to emerging infectious diseases (ID) outbreaks, with each mode triggering specific measures and actions in response to the emerging ID outbreak (see fig. 1).

The coordination of the decision of activating an outbreak Mode and the specific activities to be rapidly deployed are coordinated by the standing Outbreak Mode Committee (OMC) of PREPARE (Herman Goossens of Partner 1, Marion Koopmans of Partner 4, Peter Horby of Partner 5 and Menno de Jong of Partner 8; numbers refer to the participants table of this application). For this outbreak, following experts were added to the OMC: Communication team of Partner 1, Marc Bonten and Lennie Derde of Partner 3, Chris Butler and Nina Gobat of Partner 5, and Julia Bielicki of Partner 9.

PREPARE’s OMC has been actively following the SARS-CoV-2 outbreak that was first reported in the city of Wuhan, People’s Republic on 31 December 2019 and which has been declared a Public Health Emergency of International Concern (PHEIC) by WHO on 30 January 2020. In close consultation with scientific experts from within and outside of PREPARE and in coordination with WHO, ISARIC, and others, PREPARE’s OMC decided to enter into Mode 1 (Preparation) for the SARS-CoV-2 outbreak on 22 January 2020 (see press release). Subsequently, the OMC decided to escalate to Mode 2 (Mobilisation) on 6 February 2020 (see press release).

Despite the fact that the current outbreak has been ongoing since early December, some key questions remain difficult to address e.g. how severe is this infection and how transmissible is SARS-CoV-2, to name two. Answering these questions is challenging in any early stage emerging infectious disease outbreak, and evidence for them needs to be developed through a series of linked studies that are difficult to conduct during a vast outbreak.

Concerning severity of infection, the current situation assessment suggests that SARS-CoV-2 may cause symptoms ranging from mild to critical respiratory disease, with an estimated 20% of patients diagnosed in Hubei province requiring respiratory support, of which 3% progresses to critical and an estimated case fatality hovering around 2%. However, of considerable concern is the high rate of severe infections (26%), mortality (4.3%) and hospital-related transmission (43%) in the recent study of Wang et al in JAMA (Published online 7 February). The fatal cases are skewed towards older age groups, and persons with co-morbidities, although this is not absolute. By comparison with observations made during the SARS and
MERS outbreaks, SARS-CoV-2 has similarities in its risk groups, but the case fatality rate of SARS-CoV-2 is considered to be lower. However, these estimates are surrounded with considerable uncertainty: the level of testing in this outbreak is far in excess of what has been done during SARS (arguably the best comparator disease given region and relatedness of the viruses). Also, the outbreak is still ongoing, and the level of information currently available is insufficient to draw robust conclusions. Duration of illness can be several weeks, causing a significant burden on the healthcare system of the most affected region, Hubei province.

Similar to severity, transmissibility of SARS-CoV-2 is difficult to assess. Several estimates of $R_0$ have been released, based on specific clusters, evaluation of the epidemiology of infection in travellers and their contacts, and based on modelling of the formal notifications. While there is considerable heterogeneity in these estimates, there is consensus that the current $R_0$ is well over 1, reflecting the expanding epidemic. However, transmissibility seems to be less than for example influenza, which may transmit in limited community contact, unlike the observations made for SARS and MERS where human to human transmission is fuelled by healthcare settings or other situation of close contact. SARS-CoV-2 has been seeded outside of China through infected travellers, where secondary transmissions have occurred but not lead to sustained chains of transmission. While this is clearly resulting from the stringent quarantine measures, it does suggest that the infection is stoppable, reason for the current focus of global response on containment measures. With the declaration of a PHEIC on January 30th, the WHO prompted the global community to take the risk of international spread seriously, and help China in its control efforts through enhanced preparedness, case ascertainment and containment. In the meantime, the WHO recommended to start coordinated research efforts with a forward looking agenda, preparing for the potential situation that this virus will evolve into a global epidemic.

Given the steady increase of infected patients reported globally and within Europe, we consider sustained transmission of SARS-CoV-2 within Europe is a likely scenario, that would warrant the implementation of a comprehensive targeted research response plan to the SARS-CoV-2 outbreak which is captured in this RECOVER proposal. RECOVER brings together key clinical researchers, laboratory partners, epidemiologists, social scientists and modellers from partner networks including the IMI funded COMBACTE (Combatting Bacterial Resistance in Europe, see www.combacte.eu), the IMI2/Wellcome funded VALUE-DX project (see www.value-dx.eu), ISARIC (see https://isaric.tghn.org/), REACTing (see https://reacting.inserm.fr/). RECOVER also includes the three EU reference laboratories in the WHO global response network for SARS-CoV-2 (Erasmus MC, Charité and IP see WHO Situation report 17), built on their expertise gathered through COMPARE (www.compare-europe.eu), HONOURS, EVD-LabNet, REACTing and ZAPI. Most of these networks are currently collaborating together with other projects, networks and institutes (see section 3.3 for more info) in ECRAID-Plan (European Clinical Research Alliance for Infectious Diseases, see www.ecraid.eu) with the goal to establish itself as the European single-access sustainable clinical research network for infectious diseases. Furthermore, for its clinical biology studies (See WP5) RECOVER has built in links with complementary efforts in China, led by partner 10 IPS (see WP5b).

The overall goal of RECOVER is to develop data and evidence-based knowledge on the SARS-CoV-2 epidemic, and translate these into recommendations for improved patient management and/or public health response measures.

RECOVER will focus its research on addressing the following specific objectives/research questions:

1. To determine the spectrum of illness associated with SARS-CoV-2 and the key risk factors for disease severity caused by SARS-CoV-2.
2. To determine pathogen and host mechanisms underlying disease severity and human-to-human transmissibility of SARS-CoV-2.
3. To assess how SARS-CoV-2 evolves upon widespread circulation in Europe and its impact on spectrum of illness and key risk factors (1) and disease severity and transmissibility (2).
4. To estimate key transmission characteristics of SARS-CoV-2 in Europe and to simulate the spread of SARS-CoV-2 in the population under different control scenarios.
5. To generate social and behavioural insights relevant to effective infection, prevention and control strategies and to clinical continuity planning.

6. Liaise with WHO, ECDC, national public health agencies, and professional societies to translate our research findings into patient-level and public health level outbreak response measures.

7. Leverage lessons learned in this research response effort to further strengthen Europe’s and global clinical research preparedness to future emerging infectious disease outbreaks.

In the proposal, we have focussed on studies that we expect will complement the massive research output that will emerge from China, by selecting outstanding questions as identified at the WHO Blueprint meeting on research gaps (https://www.who.int/news-room/detail/06-02-2020-who-to-accelerate-research-and-innovation-for-new-coronavirus). The proposed studies complement ongoing research in China, adding on some targeted studies in the Hefei hospital patient population, some laboratory based studies addressing key knowledge gaps, and patient-cohort questions relevant to the European population. We will address these urgent questions in a comprehensive, multidisciplinary and interacting set of research response activities, combing (i) clinical studies in primary and hospital care, (ii) epidemiological studies and modelling, and (iii) clinical biological studies (figure 2). Given the uncertainty of the course of events in the coming months, we foresee that plans may need to be realigned periodically as more information becomes available and the trajectory of spread becomes more clear. The research proposed, however, does include essential needs for preparedness, even if circulation of the virus in Europe will be limited.

Fig. 2: Overview of the main activities proposed as part of the three interacting research components in RECOVER

- Preparing essential protocols and standards for the laboratory evaluation of patient samples;
- Phenotypic characterisation of antigenic, virulence, and possible resistance traits;
- Assessing the possible role of prior coronavirus exposures to susceptibility, severity and transmissibility;
- Host transcriptome characterisation;
- Monitor evolution of the epidemic and contribute to the reference database for precision public health;
- Determining the population incidence of cross-reactive antibodies;
- Observational studies for collecting clinical data, samples and evidence in primary care and hospital care settings across Europe to assess the prevalence, severity and disease spectrum and outcomes;
- Development, validation and deployment of in-house detection assays for 2019-nCoV;
- Qualitative research on healthcare workers’ and patients’ perspectives;
- Deployment of diagnostic capabilities across study sites;
- Development and distribution of SOPs for standardised and harmonised lab-based (in-house) detection of 2019-nCoV;
- Exhaustive etiologic diagnosis of samples collected;
- Studies on viral load;
- Studying the risk of 2019-nCoV infection in contacts of confirmed cases;
- Characterising the process of household transmission;
- Estimation of parameters characterizing 2019-nCoV transmission in Europe and of the impact of existing control interventions;
- Evaluation of the impact of possible social distancing measures;
- Monitoring behavior changes;
- Nowcasting and forecasting to inform planning activities;
- Long-term patterns of circulation and implications for Public Health;
1.2 Relation to the work programme

RECOVER responds to call topic SC1-PHE-CORONAVIRUS-2020: Advancing knowledge for the clinical and public health response to the SARS-CoV-2 epidemic.

Proposals are expected to advance the knowledge on SARS-CoV-2 and its impact on infected persons, with the aim of contributing to an efficient patient management and/or public health preparedness and response. RECOVER will advance our knowledge on the key questions on severity and transmission of the SARS-CoV-2 outbreak, captured in objectives 1-4 of RECOVER:

Severity of SARS-CoV-2 disease:
- What is the spectrum of illness associated with SARS-CoV-2?
- What are the key risk factors for disease severity?
- What are the key pathogen and host mechanisms underlying disease severity?

Transmissibility of SARS-CoV-2:
- What are the key pathogen and host mechanisms underlying human-to-human transmissibility of SARS-CoV-2?
- How does SARS-CoV-2 evolve upon widespread circulation in Europe and what is its impact on spectrum of illness and key risk factors (1) and disease severity and transmissibility (2)?
- Estimate key transmission characteristics of SARS-CoV-2 in Europe and to simulate the spread of SARS-CoV-2 in the population under different control scenarios.

We have ‘frontloaded’ answers to these questions to the early stages of the RECOVER project as much as possible to have a rapid impact on patient management and/or public health preparedness and response.

Proposals must be timely, with rapid activation, to enable early and valuable outcomes to be established.
Activities of RECOVER have already started as part of PREPARE’s actions taken in Mode 1 and Mode 2 of its outbreak response. These modes have been funded so far through the existing PREPARE budgets. Activities as part of PREPARE and its partner networks included amongst others distributing standard (e)CRFs – developed by WHO and ISARIC - across its clinical network, assessing the readiness of the laboratories to detect SARS-CoV-2 in patients across its laboratory network, and reactivating sites that participated in PREPARE clinical trials. This enables us to rapidly start enrolling patients should there be widespread circulation of SARS-CoV-2 in Europe.

Laboratory activities have been started as part of the WHO reference laboratory network (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance). Charité, Institut Pasteur and Erasmus MC are members of this network, that supports WHO in the establishment of the necessary diagnostics, and provides expert advice on the virological aspects of the evolving epidemic, building from expertise from previous collaborations (EMPERIE, COMPARE, PREDEMICS, EVD-LabNet, EVAg). Upon release of the first genome sequence of the SARS-CoV-2 January 10th, a first set of diagnostic primers was developed by Charité, and shared with partners in the network for rapid validation. This was possible as all partner share experience with SARS and access to SARS-positive specimens that could be used as proxies for the SARS-CoV-2. The results of that study were shared in real-time with WHO to guide possible diagnostic requests from outside of China. The protocol was published online on the WHO site Jan 17th, and a full report was published in EuroSurveillance in January 2020. Control reagents, validation panels, and virus isolates are shared with the global community through the EVAg repository, and initial results with the screening of travelers show good performance.

In preparation of further need, serological assay development has started in all three labs, and virus isolates are available to provide gold standard reference testing (virus neutralization assays). For specificity testing, the biobank generated through PREPARE ALICE and MERMAIDS-ARI, as well as local biobanks form the
diagnostic units at Charité and EMC were searched, and panels of well-defined samples form patients infected with known human coronaviruses and other respiratory viruses have been identified.

For increased impact, proposals may wish to build on promising avenues from previous or ongoing research. RECOVER is the ‘fast-forward’ mode of a range of projects, networks and infrastructures that have been active on infectious diseases research preparedness and response, working together in PREPARE and ECRAID-Plan and linked to many other research projects (e.g. REACTing).

The RECOVER Primary Care studies will build on the ALICÈE study in PREPARE and the Primary Care studies in VALUE-Dx:

- The experience, protocol, and data capture tools used in the EU Fp7 funded PREPARE WP4 ALICÈE trial of neuraminidase inhibitors for influenza like illness (the first ever, platform, response adaptive, platform trial successfully conducted in primary care);
- The IMI2/Wellcome funded VALUE-DX study in primary care on CA-ARTI, specifically the existing Point-Prevalence-Audit Survey (PPAS) for CA-ARTI in January-February 2020. Moreover, a trial (PRUDENCE) is planned for the next two winters (2020-2021 and 2021-2022), to evaluate diagnostic point of care tests in patients with CA-ARTI; this platform trial has the flexibility to include additional interventions should a specific SARS-CoV-2 test become available;
- Our well-developed Social Science and health psychology capability and highly relevant expertise within PREPARE and VALUE-Dx. Public, patient, clinician, key stakeholder studies in PREPARE WP1 about the ethical, administrative, regulatory, and legal aspects of conducting research during outbreaks and on new and re-emerging pathogens, as well as prospectively collected data about the processes of developing and implementing protocols for studying acute respiratory infections and antimicrobial resistance in primary care in many countries.

The RECOVER Hospital study will build on the MERMAIDS-ARI study in PREPARE and the Hospital Care studies in VALUE-Dx:

- the EU Fp7 funded PREPARE MERMAIDS-ARI study (ISRCTN number 18034878): This study executed across Europe includes adults admitted to hospital or presenting in primary care with symptoms of a recent acute respiratory infection (ARI). The primary objective is to identify host and pathogen related determinants of severity of community acquired acute respiratory infections (CA-ARI) in adults. By February 2019, 1524 patients have been recruited in in 29 hospitals and 9 primary care networks in Europe;
- The IMI2 funded VALUE-Dx study in Emergency Rooms on CA-ARTI. A trial is planned for the next two winters (2020-2021 and 2021-2022). This will be an individual patient randomized trial to determine the effects of Point of Care testing for atypical bacteria and respiratory virus on patient management (hospitalization yes/no; antibiotics yes/no). The study will be performed in hospitals in south-eastern Europe, where Point of Care testing is not yet routinely implemented. These hospitals will be prepared for implementing Point of Care testing for SARS-CoV-2 in respiratory samples when available, and will be prioritized for participation in MERMAIDS-ARI2.0 (WP3).

By using these up and running operational research infrastructures, RECOVER is able to rapidly activate clinical protocols, as well as other protocols (e.g. the Clinical Characterisation Protocol, CCP) and initiate patient inclusions in a strategically selected set of clinical sites across Europe and - when needed, based on the epidemiological and clinical data collected – redirect patient inclusions to specific regions in Europe.

Relationship to the scope
RECOVER is primarily focused on the third bullet of the examples of the type of research covered by this call (see copied below for reference).

- Development of therapeutics, including monoclonal antibodies. As relevant, evidence of regulatory and ethics approvals for the investigational products included in the study(es) must be presented.
- Development of point of care diagnostics, ensuring rapid evaluation of candidates based on existing technologies, to allow for fast case detection and surveillance.
› **Clinical and epidemiological studies**, to provide data on epidemiological characteristics such as viral genotype and pathogenicity; clinical information on host susceptibility and host immune responses; risk factors for severe disease; routes of transmission and their relative importance; identification of the animal reservoir; etc.

› **Social sciences research**, to provide urgently needed answers to social dynamics of the outbreak and the related public health response.

The emphasis of RECOVER is on the third bullet: **clinical and epidemiological studies** to provide data on important questions of the SARS-CoV-2 outbreak, particularly for Europe. We address all aspects mentioned under bullet three, except for identification of the animal reservoir. For details we refer to WPs 2, 3, 4, 5 and 6.

In RECOVER we have also included **social sciences research** including:

› Survey of public views on understanding public perception of risk; public trust in health professionals, in governments, and in science; and in science; public willingness to take part in clinical research and public notification and consent preferences (for details see WP1 and WP6). In collaboration with colleagues working on social media monitoring (VEO, SoNAR-Global), we will also include relevant questions aligned with their needs regarding sources most widely accessed.

› Interviews with health professionals and patients to understand approaches to healthcare delivery by clinicians and help seeking and prevention behaviours by patients, to understand perceptions during, rather than after, an outbreak (WP2);

› Surveys of healthcare workers as part of our clinical studies in primary care (WP2) and hospital care (WP3).

To enable developing effective clinical continuity plans, public health and clinical service managers need information about patient help seeking behavior in order to identify and anticipate patient health needs and develop effective community strategies that would encourage patients to self-triage. In addition to a rapid, rigorous description of patients’ clinical presentation, management and illness outcomes, responding to SARS-CoV-2 effectively from a community care perspective will require an understanding of the perceptions, beliefs, and actions taken, by patients and the public across various jurisdictions, mindful that reactions may vary by culture, locally available health services and local risk communication strategies. We also need to understand the views and experiences of health professionals regarding perceptions of risk, delivering care to infected and potentially infected patients, working while many colleagues may be sick or off work, their challenges with implementing guidance or imposed measures regarding testing, pharmaceutical and non-pharmaceutical interventions, and motivations to provide care. A ‘bottom-up’ understating of such issues is critical to understand how best to support this essential workforce during the SARS-CoV-2 epidemic.

We will conduct social science research alongside clinical research activities in real time. Working in this responsive way, we aim to ensure that rapidly emerging insights can feed into response measures. Retrospective interviews, once the outbreak is over, will be clouded by knowledge of how the outbreak evolved. Further, information captured too late will not be able to inform response actions. Capturing perceptions and experiences within context and during the outbreak, with any associated uncertainty, will be highly informative and critical to developing more effective clinical continuity and communication strategies and identifying how healthcare professionals can be best supported during SARS-CoV-2. Interview approaches will be pragmatic and adapted to consider the immediate needs of patients and healthcare professionals, and to minimise burden.

Third, part of the proposed activities also include elements of the second bullet (Diagnostics). The IMI2/Wellcome project, VALUE-Dx, is planning a trial of introducing new Point of Care (PoC) tests for Community Acquired Acute Respiratory Tract Infections (CA-ARTI) in primary care and hospital care, called PRUDENCE. PRUDENCE is planned to start in the winter of 2020-2021, and will continue during the winter of 2021-2022. PRUDENCE is designed as a flexible, platform trial which has the capability to include additional interventions, without having to start a new trial each time a new intervention emerges. Should a specific SARS-CoV-2 diagnostic PoC test become available by next winter, we will be able to seamlessly
include that test in the PRUDENCE trial for evaluation of analytic performance (accuracy) and impact on care and patient benefit. This will be highly efficient as it integrates the work of this WP2 into an existing planned trial, so will be cost-neutral, apart from an additional resource for microbiology testing. The trial in hospital care will be an individual patient randomized trial to determine the effects of Point of Care testing for atypical bacteria and respiratory virus on patient management (hospitalization yes/no; antibiotics yes/no). The study will be performed in hospitals in south-eastern Europe, where Point of Care testing is not yet routinely implemented. These hospitals will be prepared for implementing Point of Care testing for SARS-CoV-2 in respiratory samples when available, and will be prioritized for participation in MERMAIDS-ARI 2.0 (WP3).

So based on the studies described in WP4, and aligned with prioritisation of assays through the WHO R&D blueprint activities, in case of a full scale pandemic wave, assays meeting the WHO prequalification criteria could be trialled.

Applicants should be aware that proposals funded under this expression of interest will be required to make available their research data, in accordance with the relevant option of Article 29.3 of the H2020 model grant agreement. All clinical and research data will be quickly shared with ECDC, WHO and other relevant organisations. All clinical data will be stored in the a central data repository of the clinical data management system which also serves as the central data management system of the clinical studies conducted in PREPARE, COMBACTE and VALUE-Dx (See WP4). We will make relevant data available to be stored in the Global SARS-CoV-2 Clinical Data Platform of WHO. Sequence data will be shared through GISAID, and raw sequence read through the European nucleotide archive if possible (in view of patient privacy). Draft results when relevant for public health action will be shared ahead of publication with WHO. Journals have agreed to provide SARS-CoV-2 publications as open access and the consortium will abide by this. In compliance with article 29.3 all necessary measures will be put in place to make it possible for third parties to access, mine, exploit, reproduce and disseminate - free of charge for any user - the following (respecting confidentiality and data privacy regulations):

- the data, including associated metadata, needed to validate the results presented in scientific publications as soon as possible, within 30 days in conformity with Article 29.3 (option c);
- other data, including associated metadata, as specified in the data management plan;
- provide information — via the repository — about tools and instruments at the disposal of the beneficiaries and necessary for validating the results (and — where possible — provide the tools and instruments themselves).

The use of harmonised protocols in collaboration with other actors is recommended

The protocol for the RECOVER WP2 Primary Care study we will build on the ALIC4E study in PREPARE and the Primary Care studies in VALUE-Dx as described above.

The RECOVER WP3 Hospital Care study will be conducted in two Phases (see section 1.3 on methodology and the annexed Clinical Study template). In Phase I this study leverages the network, protocol and procedures applied in the MERMAIDS-ARI observational study on severe ARI to allow for a rapid initiation of the study. MERMAIDS-ARI is the only existing infrastructure for protocolized sample collection of patients suspected of SARS-CoV-2 infection in ambulatory care. Enrolment of patients with CA-ARTI will – when the outbreak is in Europe - yield patients with SARS-CoV-2 infection and patients with ARTI caused by other pathogens or with no documented etiology. The latter will act as the necessary controls in some of the pursued epidemiological studies.

Phase II of WP3 is an expansion of the number of sites and countries using a MERMAIDS-ARI 2.0 protocol that is based on the ISARIC- Clinical Characterisation Protocol (CCP) model, aligned to the existing MERMAIDS-ARI protocol, and will allow adaptation, based on evolving scientific insights during the outbreak. ISARIC has developed, with WHO, generic tools to capture standardized clinical data and clinical samples from patients with novel, emerging or high threat pathogens. These tools have been developed over several years, used in previous outbreaks, and have undergone extensive peer and ethical review. These tools include a standardized case record form (CRF) which can capture standardized, anonymous clinical
data as part of a research protocol or as part of clinical audit or public responses. In response to the SARS-CoV-2 outbreak, ISARIC worked with WHO to supply a rapid adaptation version of the CRF modified for SARS-CoV-2. This CRF was released widely by ISARIC and WHO in January 2020. It was also disseminated through the COMBACTE and PREPARE networks in early February as an early response activity. ISARIC also has a generic clinical characterization protocol (CCP) that requires patient consent and, in addition to the standardized CRF, allows for collection of sequential biological samples to characterize the extent and duration of infectivity, immunological responses and other important parameters. The CRF and CCP were implemented by REACTing upon identification of the first confirmed cases in France on 24 January.

The CCP protocol has been developed as a response to the epidemics of SARS, H5N1, and the 2009-10 influenza pandemic and has been released as an “open-source” research protocol, free for anyone to use or modify, supported by the World Health Organization (WHO) and is designed for any severe or potentially severe acute infection of public health interest. The protocol enables data and biological samples to be collected rapidly in a globally-harmonised manner.

The use of standardised or harmonised protocols is equally important at the level of laboratory testing and is discussed and agreed in the WHO reference laboratories for SARS-CoV-2. In WP4 and 5, activities that contribute to diagnostic preparedness will be aligned with the WHO standards and guidelines where possible. For the development of serological assays, the use of standards for assay comparison is critical, but has been very difficult to achieve for instance for MERS antibody testing. WP5 aims to produce a panel of immortalized B cells with reactivities representative of the serum antibodies found in patients, and a spin-off of that can be the use of a produced these as standards for assay comparison.
1.3 Concept and methodology

RECOVER’s research response plan addressing the project objectives listed in section 1.1 above, is organised into three highly interrelated clusters of research activities:

- **Clinical Research**: clinical observational research studies in primary care (WP2) and hospital care (WP3) across Europe collecting valuable clinical data and samples feeding into the laboratory work (WP4 and 5) and epidemiological modelling (WP6);
- **Clinical Biology**: advanced laboratory studies on key pathogen and host mechanisms underlying diseases severity and transmissibility (WP5);
- **Epidemiology and modelling**: including contact and household studies, mathematical models, nowcasting and forecasting (WP6).

The research response in RECOVER is tiered into three phases of escalating research response effort (Fig. 3), with each phase triggered by a decision by the RECOVER Governing Board, acting as the Outbreak Mode Committee (OMC) for the SARS-CoV-2 outbreak (see also section 3.2). We have chosen to develop a two-year project, with the emphasis of the work in year one, which would allow us to leverage the clinical studies in VALUE-Dx, should this be needed.

![Fig. 3 Tiered approach in RECOVER’s research response to SARS-CoV-2](image)

Fig. 3 Tiered approach in RECOVER’s research response to SARS-CoV-2, with the research in RECOVER divided into three phases, with each phase adding new or extended research by RECOVER. The length of the Mode 2 and Mode 3 boxes does not reflect the timing of the modes over the total 24 months project duration, e.g. if needed, RECOVER can decide to enter to Mode 3 on for example 13 February and decide to trigger Phase II on or example 14 February.

Before the eventual start of RECOVER on 12 February 2020, various research preparations have already been implemented in response to the SARS-CoV-2 outbreak by all partners involved, as part of Outbreak Mode 1 for PREPARE (entered on 22 January), and as part of various other networks (see section 1.2). These efforts were further intensified in Outbreak Mode 2 (entered on 6 February). Each work package in RECOVER starts out in Mode 2 with its activities as part of Phase 0, implementing part of their research tasks in anticipation of widespread and sustained transmission of the SARS-CoV-2 in Europe. If and when the RECOVER Governing Board decides to enter into Mode 3 (Research Response), Phase I will kick in for all WPs, triggering additional described research tasks. Phase II, if and when decided upon by the RECOVER Governing Board, based on the development of the n2019-CoV outbreak in Europe, will trigger the escalation of the clinical studies to a larger selection of clinical sites. **Note that the decision by the RECOVER Governing Board to enter into Mode 3 could coincide with the decision to go into Phase II for the clinical studies.**

The overall concept and approaches for each of the research work packages in RECOVER per Phase are described in the following paragraphs and further detailed into tasks and deliverables in the section 3.1 Work plan tables.
**Clinical research studies in Primary Care and Hospital Care across Europe**

We will start observational clinical studies in primary care (PC) settings and in hospital care (HC) settings across Europe. Fig. 4 depicts the core aspects of both studies.

**Primary Care**
- **Phase I**
  - Roll-out of VALUE-Dx point Prevalence Audit protocol in up to 20 PC networks across Europe.
- **Phase II**
  - Roll-out of adapted VALUE-Dx primary care study protocol (PRUDENCE) in up to 10 primary care networks across Europe.
  - Option to evaluate PoC diagnostics (funded through VALUE-Dx).

**Hospital Care**
- **Phase I**
  - Activation of the MERMAIDS-ARI protocol in 9 Primary Care networks with more intensive sampling and in 25 MERMAIDS-ARI hospital sites.
- **Phase II**
  - Roll-out of MERMAIDS-ARI 2.0 protocol aligned with the ISARIC CCP protocol in additional hospital settings – excluding paediatric centers: 30 within 2 months, 50 within 5 months.
  - Continuation of MERMAIDS ARI protocol in Primary Care.
  - Option to evaluate novel therapeutics against SARS-CoV in hospital settings across Europe in REMAP-CAP Adaptive Platform Trial (funded by PREPARE until 31/1/2021).

**Fig. 4: Summary overview of the clinical studies proposed in RECOVER**

In Phase I, both clinical studies will be started in a strategically selected set of primary care and hospital sites across Europe, building on the clinical studies conducted as part of VALUE-Dx and PREPARE (MERMAIDS-ARI). If and once sustained transmission of the SARS-CoV-2 occurs in Europe, RECOVER will trigger Phase II and scale up to those regions in Europe where the most (severe) cases are being reported. This will ensure that we enrol as many patients and patient data as possible in the study duration.

The clinical studies of RECOVER will be conducted in the clinical research network established as part of COMBACTE, PREPARE, and PENTA and currently embedded in the ECRAID-Plan initiative. This ‘warm-base’ clinical research network includes **primary care settings** (general practitioners), **hospital settings** (including emergency rooms (ERs) and intensive care units (ICUs), and **laboratories**. ECRAID’s European clinical research network is **globally connected** and can facilitate access to clinical sites and patients from clinical research networks outside of Europe, directly (e.g. ALERT, PANDORA in sub Saharan Africa and the Zika networks in Latin America) and through its strategic partners such as ISARIC.

- The **primary care network** of ECRAID consists of over 600 **primary care sites in 19 European countries**. The network has its origin in the GRACE study, funded by the European Commission. It functions as the network for the primary care studies in PREPARE and VALUE-Dx.

- The **hospital care network** of ECRAID consists of over >1,000 **hospital sites in 42 European countries**. The network has its origin in the COMBACTE-CLIN-Net project, funded by IMI. It also functions as the network for the hospital care studies in PREPARE and VALUE-Dx.

The clinical research sites are supported by a **European network of clinical laboratories of more than 800 diagnostic microbiology labs in 42 European countries** based on the laboratory network established in COMBACTE (COMBACTE LAB-Net) and currently functioning as the supporting lab network in PREPARE and VALUE-Dx (WP4).

**RECOVER Primary Care study: A prospective, observational study of community acute respiratory tract infection (CA-ARTI) in Primary Care settings across Europe (WP2).**

When new infections emerge in developed countries, most of the initial information about the illness usually comes from hospitalised, severe cases, and in the early phases, only those suspected of being at high risk of infection are tested for the disease. This means that an early, reasonable estimate of the prevalence, disease spectrum and severity, and outcomes is difficult to establish, as the mild and unsuspected cases are included in the ‘denominator’ of estimates. Many cases (and carriers) will be asymptomatic or have mild illness. Mild
and moderate cases will usually make contact with primary care as the ‘first port of call,’ where 95% of health problems are typically managed. Strong and effective primary care research infrastructure will form the foundation of a ‘living’ description of the epidemic as it evolves, contributing to informing planning, policy, communication and clinical management of the pandemic. The SARS-CoV-2 represents a threat to the people of Europe and worldwide. Effective management of the epidemic requires accurate estimation of the prevalence, the clinical presentation and illness spectrum, and outcomes of the infection, not only in hospitals, but also in primary care. It is also important to capture the associations between prevalence and outcomes with health service provision that differ markedly between European countries. An in-depth understanding of the perceptions, based on rapid and rigorous social science research, of healthcare professionals, patients and the public, within outbreaks, is essential to developing effective risk communication and care service delivery strategies. Finally, to be able to manage the epidemic effectively, the introduction of rapid tests at the first port of call is of upmost importance.

The RECOVER Primary care study will be implemented in three phases, depending on if and how the SARS-CoV-2 outbreak unfolds in Europe (see fig. 5):

**Fig. 5:** Summary overview of the primary care study activities and their essentials by phase. The length of the Mode 2 and Mode 3 boxes does not reflect the timing of the modes over the total 24 months project duration, e.g. if needed, RECOVER can decide to enter to Mode 3 on for example 13 February and decide to trigger Phase II on or example 14 February.

**The overarching objectives of the primary care study are:**

- To establish the prevalence (proportion testing positive), disease spectrum, severity and predictors of complications from novel 2019 coronavirus infection (SARS-CoV-2) in primary care selected European countries;
- To explore primary care patient and primary care healthcare professionals’ perspectives on the coronavirus epidemic in selected European countries;
- To explore the opportunity of testing new point-of-care diagnostic for SARS-CoV-2 in an IMI/Wellcome planned primary care trial already planned to start in the winter season 2020/21 as part of VALUE-Dx.

**In Phase I**, the primary care study will start out with an enhanced Point Prevalence Audit study based on the IMI2/Wellcome funded VALUE-DX WP4 study of patients presenting to primary care with acute community acquired respiratory tract infection (CA-ARTI) in 18 European countries. This study has been classified as audit (non-research), so ethics approval or individual patient consent is not required. Data are being collected anonymously, and in the space of five weeks, we have registered over 3500 patients with CA-ARTI and are describing its presentation, management and treatment. Each of the 18 countries have been asked to register at least 240 and up to 350 patients until the end of March 2020, and half of the networks have
already met their target. As this ongoing PPAS does not carry permissions for taking individual patient consent, there is no provision for microbiological or other sampling, and patient outcomes are not measured.

For RECOVER, we propose to extend and modify this study to allow us to take individual consent when we register patients. This consent would allow us to enhance the PPAS to capture and obtain:

› Additional SARS-CoV-2 outbreak relevant data that will include a minimum data set of the items from the WHO (ISARIC) eCRF and CCP protocol to allow comparison with hospitalised cases and with surveillance programs;
› A throat and/or nasal swab for research purposes;
› Data from patients’ medical records and from patients themselves about subsequent health care utilisation, prevention strategies, antiviral and antibiotic use, and clinical outcomes like complications (including hospitalisation, new or worsening symptoms, pneumonia), or death;
› Permission to approach contacts of confirmed positive cases to obtain additional data in one selected country to feed into WP6 (contact traceability);
› Data about clinician and patient perceptions of risk, delivery of care and public health messaging, and associated self-care and prevention behaviours.

In Phase II, the Primary Care study will roll out an adapted version of VALUE-Dx PRUDENCE trial that involves introducing new POC tests for CA-ARTI in primary care and is planned to start in the winter of 2020-2021, and continue during the winter of 2021-2022. This trial, called PRUDENCE, is being designed as a flexible, platform trial which has the capability to include additional interventions, without having to start a new trial each time a new intervention emerges. Should a specific SARS-CoV-2 diagnostic point of care test become available by next winter, and if the SARS-CoV-2 shows seasonality, we will be able to seamlessly include that test in the PRUDENCE trial for evaluation of analytic performance (accuracy) and impact on care and patient benefit. This will be highly efficient as it integrates the work of this WP2 into an existing planned trail, so will be cost-neutral, apart from an additional resource for microbiology testing.

This Phase II study will build on:

› Our existing PPAS for CA-ARTI in January-March 2020 (VALUE-Dx WP4 PPAS);
› The experience, protocol, and data capture tools used in the PREPARE WP4 ALIC4E trial of neuraminidase inhibitors for influenza-like-illness (the first ever, platform, response adaptive, platform trial successfully conducted in primary care);
› Already planned and funded protocol development and implementation of the VALUE-Dx WP4a primary care trial, PRUDENCE, testing new POC diagnostics for CA-ARTI to be conducted in the winters of 2020-2022;
› Our well-developed Social Science capability and their highly relevant expertise gained within PREPARE and VALUE-Dx;
› Public, patient, clinician and key stakeholder studies in PREPARE WP1 about the ethical, administrative, regulatory, and legal aspects of conducting research during outbreaks and on new and re-emerging pathogens;
› Prospectively collected data about the processes of developing and implementing protocols for studying acute respiratory infections and antimicrobial resistance in primary care in many countries.

Perceptions and experiences of healthcare professional and patients to inform risk communication strategy
Emerging evidence regarding clinical features of SARS-CoV-2 suggests that many patients, including children, will present with mild illness and this is likely to result in a surge of patients asking for examination and treatment in community care settings. Furthermore, information and the inevitable "infodemic" of misinformation is circulating, creating anxiety among the general public. This is likely to lead to a surge on community-based health services. Identifying strategies to divert patients by anticipating their needs and directing them to appropriate services will be key to managing patient demand.
To develop effective clinical continuity plans, public health and clinical service managers need information about patient help seeking behavior in order to identify and anticipate patient health needs and develop effective community strategies that would encourage patients to self-triage. It follows therefore that, in addition to a rapid, rigorous description of patients’ clinical presentation, management and illness outcomes, responding to SARS-CoV-2 effectively from a community care perspective will require an understanding of the perceptions, beliefs, and actions taken, by patients and the public across various jurisdictions, mindful that reactions may vary by culture, locally available health services and local risk communication strategies. We also need to understand the view and experiences of health professionals regarding perceptions of risk, willingness to delivering care to infected and potentially infected patients, working while many colleagues may be sick or off work, their challenges with implementing guidance or imposed measures regarding testing, pharmaceutical and non-pharmaceutical interventions, and motivations to provide care. A ‘bottom-up’ understating of such issues is critical to understand how best to support this essential workforce during the SARS-CoV-2 epidemic, mitigating burnout among clinicians post-epidemic and ensuring clinical continuity.

Conducting this work alongside the clinical research activities in real time is important as retrospective interviews, once the outbreak is over, will be clouded by knowledge of how the outbreak evolved. Further, information captured too late will not be able to inform response actions. Capturing perceptions within context and during the outbreak, with any associated uncertainty, will be highly informative and critical to developing more effective clinical continuity and communication strategies and identifying how healthcare professionals can be best supported during SARS-CoV-2. Interview approaches will be pragmatic and adapted to consider the immediate needs of patients and healthcare professionals, and to minimise burden.
RECOVER Hospital Care study: A prospective, observational study of community acute respiratory tract infection (CA-ARTI) in Hospital Care settings across Europe (WP3).

RECOVER will implement a hospital study on the clinical epidemiology of severe SARS-CoV-2 infections focusing on patients presenting to the Emergency Room, or that are being hospitalized for suspected or confirmed SARS-CoV-2 infections.

The overarching objectives of the Hospital care study are:

- To establish the frequency, disease spectrum and severity, clinical features, management, risk factors, spread and outcomes of novel 2019 coronavirus infection (SARS-CoV-2) in Hospital Care in selected European countries;
- To explore hospital care healthcare professionals’ perspectives on the coronavirus epidemic in selected European countries;
- To identify index subjects for contact tracing and household studies that will deliver the samples and data for the biological and modelling studies in WPs 5 and 6;
- To explore opportunities of testing novel diagnostics for SARS-CoV-2 in an IMI/Wellcome funded hospital care trial already planned to start in the winter season 2020/21 as part of VALUE-Dx;
- To explore opportunities of testing new therapeutic agents and/or supportive therapy for severe SARS-CoV-2 infection in the ongoing REMAP-CAP trial as part of PREPARE.

Like the Primary Care study, the hospital study is set –up in three consecutive phases (see fig.6):

- **Phase I** (if sustained transmission)
  - activation of the MERMAIDS-ARI protocol (≥ 18 yrs of age);
  - 9 Primary care networks and 29 hospital sites across Europe;
  - Ready for pt. enrollment in 2-3 weeks after go for Mode 3
  - Preparations for Phase II

- **Phase II** (if sustained transmission)
  - Roll out of MERMAIDS-ARI 2.0 protocol aligned with the ISARIC CCP protocol in hospital settings of COMBACTE, CLIN-NET, VALUE-Dx and PENTA-ID (latter for pediatric centers);
  - Continuation of Phase I study in Primary Care;
  - Hospital sites activation MERMAIDS 2.0

- **Optional and partially funded through PREPARE until 1/2/2021 and other sources:**
  - Evaluation of novel therapeutics against 2019-nCoV in hospital settings across Europe in REMAP-CAP Adaptive Platform Trial

**Outbreak Modes**

- **2** Clinical Research Mobilisation Mode: Funded through PREPARE
  - 6 February 2020
  - After go by RECOVER Governing Board to enter into Mode 3

- **3** Clinical Research Response Mode: Funded through RECOVER
  - Go by RECOVER Governing Board based on development of the 2019-nCoV Epidemic per region

**Fig. 6: Summary overview of the primary care/hospital care study activities and their essentials by phase. The length of the Mode 2 and Mode 3 boxes does not reflect the timing of the modes over the total 24 months project duration, e.g. if needed, RECOVER can decide to enter to Mode 3 on for example 13 February and decide to trigger Phase II on or example 14 February.

In Phase I this study leverages the network, protocol and procedures applied in the MERMAIDS-ARI observational study on severe ARI to allow for a rapid initiation of the study. MERMAIDS-ARI involves 29 hospitals and 9 primary care networks in Europe. This study was designed to generate insights into the development of severe ARI by detailed investigations of host- and pathogen-related factors in patients across the clinical spectrum of disease, ranging from mild (primary care) to moderate or severe (hospital) illness. Enrollment of patients with CA-ARTI was recently completed, but local contracts and ethical approvals at study sites are still in place and can therefore be rapidly reopened, with minor amendments to the current study protocol. Sampling and data collection largely overlaps with the phase II CCP-aligned hospital study (see below) providing opportunities to merge data and samples collected in both phases. Through this reactivation of MERMAIDS-ARI we secure rapid initiation of data and (limited) sample collection in primary care and hospital care. We anticipate to enroll the first patients in the study within 2-3
weeks after the decision to enter into Mode 3. These timelines would be impossible to meet for a new study set-up, considering turnover times for local contracting and approval procedures. This is the reason why we have decided to distinguish the reactivation of sites (Phase I) from the expansion of sites (being Phase II). It was also decided to include both the 29 hospital and 9 primary care networks, because of the unique aspect of combined data and sample collection in both hospital and primary care domains. WP2 study activities in primary care are focused on observational data of a large population without extensive sample collection. MERMAIDS-ARI, therefore, is the only existing infrastructure for protocolized sample collection of patients suspected of SARS-CoV-2 infection in ambulatory care. Enrolment of patients with CA-ARTI will – when the outbreak is in Europe - yield patients with SARS-CoV-2 infection and patients with ARTI caused by other pathogens or with no documented etiology. The latter will act as the necessary controls in some of the pursued epidemiological studies.

**Phase II** of WP3 is an expansion of the number of sites and countries participating in an observational study to improve geographical coverage in Europe, to enhance accumulation of enrolled cases, to allow more and targeted biological sampling needed for WP5 and WP6, and to allow enrolment of children (non-eligible in Phase I). This part is, therefore, named **MERMAIDS-ARI2.0**. The MERMAIDS-ARI 2.0 protocol will be based on the ISARIC-CCP model, aligned to the existing MERMAIDS-ARI protocol, and will allow adaptation, based on evolving scientific insights during the outbreak. The clinical research infrastructures of COMBACTE, CLIN-NE, VALUE-Dx and PENTA-ID will be used for Part II site selection. This way, EU and IMI investment efforts are optimally leveraged in support of fast and cost-efficient establishment of a clinical network with broad European coverage providing access to a large patient population across all age groups and differing healthcare environments. The preparations for initiating Phase II WP3 activities in the new study sites will start immediately after proposal submission by protocol finalization, site selection, IRB submissions and contracting. The ambition is to have **30 sites activated within 2 months after entering Mode 3 and 50 sites within 4-5 months**. Enrolment of patients will be based on documented SARS-CoV-2 infection. Therefore, sites with capability of rapid testing for this infection will be prioritized in the site selection process. Importantly, eligibility for phase II includes patients with nosocomial acquisition of SARS-CoV-2, as this appeared to be an important transmission route in Chinese hospitals according to the recent study by Wang et al in JAMA (published online 7 February).
Clinical Biology studies (WP5)
The clinical biology studies in RECOVER will be conducted by Europe’s leading laboratories on Coronavirus research at Erasmus MC, Charité and Institut Pasteur, who are all members of the European SARS-CoV-2 referral laboratories in the global network of WHO. In addition, these studies will build on established analysis pipelines developed by laboratories in the context of PREPARE. They will collaborate in a fast-track essential clinical biology work package (WP5) that addresses key outstanding clinical and public health questions through a combination of clinical biology studies as summarised in fig. 7.

**Fig. 7:** Summary overview of the clinical biology study activities by phase. The length of the Mode 2 and Mode 3 boxes does not reflect the timing of the modes over the total 24 months project duration, e.g. if needed, RECOVER can decide to enter to Mode 3 on for example 23 February.

The overall goal of these studies is to develop the tools needed for the clinical studies described in this proposal, and to provide answers to key outstanding questions on SARS-CoV-2 severity, and transmissibility during evolution of the current epidemic and in the European context. This work will build from expertise in MERS, SARS, and human coronaviruses, and refocus the tools developed for studies of these pathogens in PREPARE, COMPARE and ZAPI to include the SARS-CoV-2. Key outstanding questions addressed specifically in WP5 are: how severe is disease caused by SARS-CoV-2 compared with SARS in animal models, and can we use animal models for a standardised way of comparing transmissibility? What is the tissue tropism of SARS-CoV-2 and how does that translate to ability to diagnose and measure antibodies; 3) how stable is SARS-CoV-2 in patient samples and in the environment and how can that information be translated for understanding transmission routes, risk assessment and infection prevention guidelines? (How) do SARS-CoV-2 genomes evolve with time and does that affect any of its properties? Is there some degree of immunity in the population from exposures to seasonal influenza viruses? We will adapt and employ multi-antigen serology, pathogen genomics and bioinformatics, host B-cell antibody profiling and transcriptome analysis. Biobanked samples and available transcriptome data from well characterised patients infected with other respiratory pathogens, including known human coronaviruses from PREPARE, and other networks (e.g. REACTing), and the international Pasteur network, as well as serum samples from experimentally infected or immunised animals will serve as a reference set, allowing rapid determination of common and unique markers for SARS-CoV-2 infection. WP5 is aligned with similar studies ongoing in China, through partner 10 that serves one of the designated hospitals of the Chinese Academy of Sciences network, reserved for patients infected with the SARS-CoV-2. The cross-European collaboration in WP5 and the WP5B-China interaction will focus on bridging data generated in China with observations in Europe, through comparison of assays used, and exchange of assays standards.
In Phase I of RECOVER we will further expand on the work done at the labs by implementing patient-based lab studies involving

› Preparing essential protocols and standards for the laboratory evaluation of patient samples collected through the WP2,3 and 6 studies;
› Providing characterisation of viruses through in vitro and in vivo studies, to allow phenotypic characterisation of antigenic, virulence, and possible resistance traits for rapid risk assessment purposes;
› Assessing the possible role of prior coronavirus exposures to susceptibility, severity and transmissibility.

In Phase II, if and when there is widespread circulation of SARS-CoV-2 in Europe, the lab studies will be extended with:

› Host gene expression profiling analyses to characterize the host transcriptome in patients with SARS-CoV-2 in order to understand development of severe disease and identify predictive biomarkers for severity and potential targets for therapeutic intervention;
› Population-based studies to monitor evolution of the epidemic and contribute to the reference database for precision public health by characterization of viral genomes and phenotypic traits and to determine the population incidence of cross-reactive antibodies in selected sites in Europe in liaison with the ECDC coordinated seroprevalence study.

Link to clinical biology studies in China led by IP Shanghai (WP5B)

We will link our clinical biology studies to similar studies done in China, led by IP Shanghai-Hefei (WP5B). These activities will be funded through the State Basic Research Development Program of China (MOST). These clinical biology studies are described in WP5B and are a collaboration between WP5 and the Pasteur Institute of Shanghai (member of the Institut Pasteur Asia Pacific Network) which has agreed working relationships with and is embedded in the Chinese Academy of Science Affiliated Hospital in Hefei. The proposed research is aligned with the clinical biology studies by RECOVER in WP5. In case of successful funding, their partnership is eligible for matching funding from China through bilateral treaties with the EU and Ministry of Science and Technology of the People’s Republic of China (MOST). IP Shanghai provides the laboratory research support for the Chinese Academy of Science Affiliated Hospital in Hefei, which is a designated centre for the case of patients infected with SARS-CoV-2. Anhui province at present has 800 patients, and is expecting to see more given the local epidemiology at present, although stringent quarantine measures have been imposed, aiming to contain the spread of SARS-CoV-2.
Transmission, Epidemiology and Modeling studies (WP6)

Decision makers and planners managing the response to the SARS-CoV-2 epidemic need to be supported by sound assessments of risks, detailed evaluations of the likely impact of the control strategies they could implement, epidemic nowcasting and forecasting. RECOVER will therefore provide a range of data and analytical results to guide the Public Health response.

In the absence of vaccine, the spread of SARS-CoV-2 can only be mitigated via non-pharmaceutical interventions that reduce the risks of forward transmission. In 2003, the SARS epidemic was contained thanks to a strategy based on the isolation of cases and their symptomatic contacts. In contrast, to block the spread of SARS-CoV-2, Chinese authorities have started implementing much more drastic social distancing measures with the quarantine of whole cities and regions, school and workplace closures and cancellations of mass gatherings. As more cases get detected in Europe, European policy makers will need to determine which combination of control measures they plan to use in their countries (i.e. will a SARS-like strategy be sufficient? Is a more aggressive response warranted?); and how they may modify their Public Health response depending on the evolution of the situation. Europe is better prepared than China was in December 2019 and is not currently experiencing widespread transmission. So, the probability of successful containment with a SARS-like strategy is higher in Europe than it was in China. That being said, if the epidemic becomes widespread internationally, such an approach may become infeasible and additional social distancing interventions may have to be considered. To evaluate the likely impact of such interventions in Europe, it is essential to build a detailed understanding of the key transmission parameters of SARS-CoV-2 and to ascertain transmission risk factors. Such understanding is also important to determine which contacts of a case should be prioritized for contact tracing in a context where follow-up of all contacts may quickly become impossible.

![Epi studies and modeling](image)

**Phase I**
- Studying the risk of 2019-nCoV infection in contacts of confirmed cases;
- Studying household transmission of 2019-nCoV;
- Estimation of parameters characterizing 2019-nCoV transmission in Europe and of the impact of existing control interventions;
- Evaluation of the impact of possible social distancing measures on 2019-nCoV spread;
- Continued monitoring of the risk of importation of 2019-nCoV in Europe;
- Monitoring behavior changes through participative surveillance platforms.

**Phase II**
- Nowcasting and forecasting to inform planning activities;
- Determining the long-term patterns of circulation and implications for Public Health;
- Estimating key transmission characteristics of SARS-CoV-2 in Europe from detailed data documenting the transmission of SARS-CoV-2 to contacts of confirmed cases.

Fig. 8: Summary overview of the epidemiological and modelling studies by phase. The length of the Mode 2 and Mode 3 boxes does not reflect the timing of the modes over the total 24 months project duration, e.g. if needed, RECOVER can decide to enter to Mode 3 on for example 13 February and decide to trigger Phase II on or example 14 February.

Our epidemiological modelling efforts will therefore involve the following studies as part of Phase I (see fig. 8.):

- Estimating key transmission characteristics of SARS-CoV-2 in Europe from detailed data documenting the transmission of SARS-CoV-2 to contacts of confirmed cases.
Integrating these estimates into mathematical models that can simulate the spread of SARS-CoV-2 in the population under different control scenarios – so that the impact of the different control strategies can be evaluated.

In the event that transmission of SARS-CoV-2 becomes widespread in Europe and RECOVER enters into Phase II, it will be important to monitor and forecast the epidemic trajectory so as to inform planning of the response and of required resources. In this scenario we will:

- Develop tools for nowcasting and forecasting.
- Investigate the long-term implications of this emergence for Public Health.

Central management, coordination, communication and dissemination activities
The research efforts in RECOVER are supported by an overarching set of Management, Coordination, Communication, Dissemination and Engagement activities. Here we will leverage on the established processes in PREPARE and COMBACTE (currently further solidified in ECRAID-Plan).

Linked Initiatives and projects
RECOVER builds on the investments over many years in several projects and networks active in infectious disease research preparedness and response. These projects, and how they link to RECOVER are summarised in the table below:

<table>
<thead>
<tr>
<th>Linked initiative/project</th>
<th>Link to RECOVER</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREPARE</td>
<td>RECOVER originates from PREPARE. It is the research response plan to the SARS-CoV-2 epidemic developed by partners in PREPARE as part of Outbreak Mode 3. The WP2 and WP3 clinical studies build on the clinical studies conducted in PREPARE, enabling a swift initiation of patient enrolments in RECOVER. The WP4 laboratory support builds on the laboratory/diagnostic support infrastructure build in PREPARE.</td>
</tr>
<tr>
<td>COMBACTE</td>
<td>The WP3 clinical studies will be conducted in the warm-base hospital network of COMBACTE Clin-Net that also serves as the hospital network in PREPARE, VALUE-Dx (besides the COMBACTE studies themselves)</td>
</tr>
<tr>
<td>VALUE-Dx</td>
<td>WP2 and WP3 clinical studies will leverage the studies conducted in VALUE-Dx in Primary Care and Hospital Care on Community-Acquired Acute Respiratory Tract Infections.</td>
</tr>
<tr>
<td>REACTing</td>
<td>REACTing is a multi-disciplinary collaborative network of French research institutions working on emerging infectious diseases, which aims to prepare and respond to epidemics.</td>
</tr>
<tr>
<td>COMPARE/VEO</td>
<td>COMPARE and its sequel VEO aim to improve our ability to detect outbreaks, through combinations of advanced mining of public data, supplemented with targeted data collection by participation of citizen scientists, and hot spot targeted analysis of surveillance samples and patient based studies. In VEO, a digital epidemiology working group has been established, to track the infodemic. Tools developed in COMPARE will be used in RECOVER.</td>
</tr>
<tr>
<td>SONAR-G</td>
<td>SoNAR-Global is the EC-funded social sciences network for preparedness and response to epidemics. Its coordinator, T Giles-Vernick, will participate in WP 2 and 3, and will mobilize other partners and members of the network as needed to assist.</td>
</tr>
<tr>
<td>ISARIC</td>
<td>PREPARE is a member of ISARIC and will make use of the ISARIC eCRF and CCP protocol. It will leverage the global network of ISARIC to connect to other relevant research response efforts at the global level.</td>
</tr>
<tr>
<td>EVD-LabNet</td>
<td>EVD-LabNet is a network of reference laboratories specialised in emerging disease preparedness, with emphasis on arboviruses.</td>
</tr>
<tr>
<td>C4C</td>
<td>Future clinical studies in children will be conducted in collaboration with Conect4Children network, a large IMI2 funded projects involving paediatric national networks from 19 European countries with more than 300 clinical sites. The project is coordinated by PENTA.</td>
</tr>
</tbody>
</table>
1.4 Ambition

Should SARS-CoV-2 spread widely throughout Europe, the virus is likely to behave differently than in China, given different population dynamics and behaviours in Europe. Relying on evidence from China to guide management in the EU, which although useful, will not be sufficient for optimal care delivery and policy development. The way the pandemic will evolve in Europe will depend on local circumstances, population dynamics, attitudes and behaviours, and care delivery policies. Early on, we will not have a clear idea of who, in Europe, is most at risk form the novel virus, what interventions might modify the illness, and what the risk factors will be for poorer outcomes. Understanding prevalence, transmission, and risk factors for complications will be critical to context-specific, effective management of the outbreak. In any pandemic, healthcare professionals’ perceptions and the perceptions of patients and the public will evolve in response to rapidly changing circumstances and information provision. Understanding what information people are receiving, and the sources, will be critical to ensuring that risk communication and public health messages are appropriate to the circumstances at the time. The primary care studies will, for the first time, describe the prevalence, presentation, management, and outcomes of large numbers of patients presenting with acute respiratory tract infection in primary care during a time of widespread SARS-CoV-2 infection. Primary care is where most infections will be managed. Comparable data from contrasting European countries will allow within- and between-country comparisons, and an examination of how variation in help seeking, information provision, and care delivery affects the pandemic’s evolution. These studies will be a ‘world-first’ advance in the understanding of the pandemic in Europe, and will allow European research to inform health services delivery, clinical care, and risk communication and public health messaging within the pandemic itself for the benefit of European citizens.

WP3 will provide essential information on the disease spectrum and severity, clinical features, management, risk factors, and outcomes of SARS-CoV-2 infection in Europe. Although high-quality data are rapidly emerging from China, the generalizability to the European setting of such findings is currently unknown. Detailed data from European centres is, therefore, essential for informing health care workers, policy makers and European public.

WP3 will also provide essential information on the occurrence (and incidence) of nosocomial acquisition of SARS-CoV-2 infection by patients and healthcare workers, which appears to be very common in China. This aspect adds a major threat to the widespread community transmission of a new virus, as it might limit medical access for many infected patients. WP3 will, therefore, also explore hospital care patient and hospital care healthcare professionals’ perspectives on SARS-CoV-2 infection. The proposed contact tracing studies among – sporadic - patients in the early phases of the outbreak and among households during the phase of sustained transmission will provide key insights in transmission processes of SARS-CoV-2, it’s drivers and, through mathematical modelling estimate the epidemic trajectory and the potential impact of public health control measures.

Diagnostic assays with validated high sensitivity and specificity are crucial to diagnose infections, and estimate the prevalence of the SARS-CoV-2. While molecular-based assays have been developed that enable sensitive and specific diagnosis of SARS-CoV-2 infections, yet, serologic detection remains necessary and are lacking at the moment. Serologic detection of SARS-CoV-2 exposure is valuable for identifying asymptomatic cases and virus reservoirs in population screening and epidemiologic studies, as well as for contact investigations, to ensure that the full spectrum of infections is identified. Detection also aids in understanding the host immune response to the virus, identifying key viral immunogens, and mapping key neutralizing antibodies, which all lead to implementing appropriate preventive and therapeutic measures. Therefore, validated serologic assays are urgently needed and are lacking at the moment.

In addition to supporting clinical studies that – by their design- will generate reliable estimates of the disease surveillance pyramid and therefore of the overall severity, the laboratory studies bring essential new
findings addressing key knowledge gaps: the SARS-CoV-2 viruses are related to SARS, which in turn groups with betacoronaviruses. Antigenically, SARS-CoV-2 are quite distinct form other coronaviruses that circulate in humans, and therefore the level of cross protection from prior exposures through S1 binding neutralising antibodies and antibodies to the receptor-binding domain on S1 will be very low.

While the CoV spike S1 and the RBD are the main targets for protective antibody and (therefore also preferred targets for therapeutic antibodies and vaccine-induced antibodies), they are highly divergent among different CoVs providing virus specific protection. The spike S2 domain and the N protein are more conserved, and thus adaptive immune response directed against these proteins can potentially lay the basis for a more broadly-acting coronavirus response. Evidence for cross reactive immune responses against different CoVs is still limited. Convalescent SARS-CoV patient sera weakly neutralized MERS-CoV and SARS-S reactive antisera showed low level neutralization of MERS-CoV. This suggests that there may be cross reactivity with nCpV as well, as these viruses are more closely related to SARS than MERS CoV. Extra-RBD S1 or S2 epitopes could be responsible for this effect, as some neutralizing epitopes have been identified in these regions of the S protein. Non-neutralizing conserved epitopes should also be sought, as non-neutralizing S2 epitopes were found to be protective against MERS-CoV. These may not be as immunodominant as the RBD epitopes but could provide some level of protection. Addressing this question is important given the currently skewed age distribution of SARS-CoV-2 cases and deaths, suggesting some degree of protection in lower age groups.

Whole-genome sequencing allows to describe the genetic characteristics of the virus and its evolution. Timely global sharing of whole-genome sequences through the GISAID database enables monitoring virus evolution understand features of spatio-temporal temporal spread of the virus and chains of local transmission, and monitor virus adaptation upon circulation in the human population. Sequence determination from specimens from different shedding sites and in the course of disease will provide information about evolution of the viral population within the host, enable identification of potential virulence markers through comparison between mild and severe cases, and emergence of markers of resistance to antiviral treatments when applied. Specific viral genetic traits will then be correlated to phenotypic characteristics generated in in vitro and in vivo models.

Another unique asset in this consortium is the expertise on standardised transmissibility studies in animal models. This model has been validated extensively to serve as indicator of potential mammalian transmissibility of respiratory viruses. To study SARS-CoV-2 transmission, a modified version of the previously described influenza A virus ferret transmission set-up will be used. This set-up consists of two clear polymethyl methacrylate cages of different sizes. Donor ferrets and direct contact recipients will be housed in separated by two stainless steel grids 10 cm apart to prevent direct contact but still allow airflow from the donor ferret to the airborne recipient ferret. These transmission cages allow the experiment to be conducted in negatively pressured isolators in the BSL3 facility, with HEPA-filtered airflow <0.1 m/s. Using this study design, SARS-CoV-2 transmissibility can be directly compared with that of other respiratory viruses for which we have obtained data with the same model.

Host gene expression profiling analyses provide detailed genome-wide insights into respiratory and systemic host responses during SARS-CoV-2 infection. Comparison of responses during mild and more severe disease manifestations allows us to understand development of severe disease and to identify predictive biomarkers of severity and potential host-related targets for intervention. In addition, comparison to infections with other respiratory viruses will help to understand whether and to which extent SARS-CoV-2 behaves differently than other common respiratory pathogens, including human coronaviruses. The large amount of gene expression profiling data generated as part of the PREPARE MERMAIDS-ARI study, which was designed as a sufficiently powered cohort to enable stratified analyses of host transcriptomes across a range of pathogens as well as of underlying comorbidities, will allow such comparisons. Illustrating the strength of MERMAIDS-ARI, preliminary analyses identified expression profiles predictive of influenza severity as well as set of classifier genes that distinguishes a range of individual respiratory viral infections, including influenza, rhinoviruses, RSV and coronaviruses.
2. IMPACT

2.1 Expected impacts

All proposed studies have been aligned with the urgent research agenda as developed at WHO February 11 and 12, through participation of 5 experts participating in this consortium. The alignment with the global strategic goals is therefore ensured, as they will continue to participate in these coordinated research meetings, share findings from the proposed studies, and inform the consortium leadership of relevant developments that may warrant adaptation of study designs in our consortium.

The information derived from the clinical, social science, laboratory, and modelling studies will inform, during the epidemic itself, planning and care delivery strategies to modify the evolution of the epidemic. Understanding the prevalence, clinical features, risk of poor outcome, population dynamics and spread, and perceptions of healthcare professionals, patients, and the public, during the epidemic itself, will be critically useful to ensuring optimal management both in terms of patient care and to clinical continuity planning.

The representation of children in RECOVER is critical for maximum impact on public health measures in response to the SARS-CoV-2 outbreak. A clear understanding of the role of children in transmission networks, including in the household, will support modelling of the impact of social-distancing measures frequently involving young people, such as school closures. Such measures need to be based on robust evidence to provide justification for their socio-economic impacts, for example parent absenteeism to provide in-home childcare. The rapid deployment of basic and or advanced diagnostic capacity developed in WP4 and WP5 to local laboratory infrastructures by providing protocols, nucleic acid controls, generation of harmonised standards for comparison of Ct values among different quantitative PCR platforms will guarantee laboratory capacity to rapidly impact individual patient management and support clinical trials on the SARS-CoV-2.

The diagnostic tools for virus detection and serology developed in WP5 as well as analyses of virus evolution will be key for monitoring the extent of the epidemic, evaluate the level of severity, and identify risk groups for severe disease. This information will serve to inform modelling (WP6) and will have a direct impact for planning of patient management. Information gathered on virus adaptation, potential emergence of reduced susceptibility to treatment options, and key phenotypic changes, will further help to update risk assessments. Furthermore, studies documenting the natural history of disease in patients with various degrees of severity, and the identification of prognostic markers will inform individual patient management, and guide treatment options. In addition, laboratory studies will generate key data about virus transmission, that could be used for rational decisions for patient discharge and management of contacts with direct impact on transmission mitigation.

The serological tools and kinetics of immune response will also be critical input for population surveys looking at incidence of infection, and we have discussed their utility in liaison with serosurveys that are being planned by public health partners in different countries, coordinated through ECDC. The sero-immunology studies provide essential information on susceptibility of persons <30 years of age in which the incidence of diagnosed infections currently is low. Understanding the contribution of these younger age groups is critical, as they are considered key drivers for epidemics of respiratory diseases. The antibody profiling data will also inform vaccine development, where concern has been raised about potential interference of pre-existing exposures to other coronavirus infections, and the need for tools to evaluate responses has been stressed. The liaison with partners based in China, serving one of the Chinese Academy of Sciences hospitals designated for care of patients with COVID-19 disease ensures harmonization of studies with ongoing work done through the Chinese Academy affiliated institutes, thus avoiding duplication of efforts.

Importantly, the inclusion of children in WP2, WP3, WP6 will allow the specific characterisation of this population in the SARS-CoV-2 outbreak. Currently, children are relatively underrepresented among patients...
with confirmed SARS-CoV-2 infection. An improved understanding whether this is due to lower infection risk, milder symptoms on infection, different care-seeking behaviour or other factors will be critical to adaptation of diagnostic and clinical management algorithms for this population.

Social science research will bring vital insights to inform effective infection, prevention and control strategies in community and hospital settings, by understanding healthcare worker knowledge regarding infection, prevention and control strategies and their confidence in enacting them. Protecting the health of all staff involved in keeping clinical services open is a top priority. In Europe, these Research from previous novel coronavirus epidemics, illustrates how healthcare worker trust in effective health systems management, and self-efficacy regarding enacting infection, prevention and control is also protective of post-event burnout. Social science research will also bring rapid insight into public health seeking behavior, trust in the overall response, and trust in science and will inform our public engagement and communication strategies. These strategies are aimed at engaging European citizens in the value and contribution of science to address the current epidemic. Through a targeted communication and impact strategy, we will ensure rapid identification of mechanisms and pipelines for sharing knowledge at the earliest stage and ensure key decision makers receive synthesized evidence in a timely way.

Through all of the above, we are confident that the research proposed will yield actionable information that is of immediate relevance to the outbreak response endeavor, in the spirit of the new model for collaborative outbreak research developed under the WHO R&D blueprint. The potential barriers to this new way of working, including the need to adapt plans with new developments, data sharing, legal and ethical barriers, publication priority etc. will be an integral part of the discussions at our consortium meetings.

**RECOVER's contribution to the public health preparedness and response in the context of the ongoing epidemic of SARS-CoV-2.**

A clear description of how this infection is spreading, the clinical and microbiological features of both mild and severe cases in the European context, and the understanding of healthcare professionals patients and the public, and where they get their information from and what their information needs are, will allow public health services to refine and target both clinical care strategies and information provision relevant to the evolving circumstances of the epidemic.

The analyses performed in WP6 will provide estimates of the key transmission characteristics of SARS-CoV-2 in Europe that are essential to guide the European Public Health response to the epidemic. Mathematical models will be used to assess the likely impact of a range of social-distancing measures such as case isolation, school and workplace closures, travel restrictions to inform strategic decision making by European leaders. Tools for nowcasting and forecasting will be developed to guide planning activities and the management of hospital resources. Finally, assessments of the long-term Public Health impact of this emergence will be performed to guide longer term planning.

**Barriers and obstacles to achieving impact**

Should cases remain sporadic and never become widespread, then characterising large numbers of cases will become inefficient and less productive. However, the 'stop-go' decision mechanism embedded in WP2 and WP3 will guard against premature triggering of the primary and hospital care studies that seek to include large numbers of cases. On the other hand, if the epidemic becomes very widespread with a high proportion of severe cases, then the research will be hard to deliver in both primary, secondary and tertiary care. Both primary care and hospital-based studies will rely on contributions from healthcare staff delivering routine care. If healthcare personnel become overwhelmed and even more short-staffed, or many healthcare staff become sick themselves, then identifying cases and recording patients data for research and surveillance purposes will become increasingly difficult and ever - lower priority. Wherever possible, we will mitigate this by having non clinical and non-health service staff doing research related tasks wherever possible. By building on successful, well function clinical networks, where much of the activity and tasks are delivered by non-clinical staff, this risk will be mitigated.
2.2 Measures to maximise impact

**DISSEMINATION AND EXPLOITATION OF RESULTS**

RECOVER aims to have an impact on the clinical management of patients in primary care and hospital care and on the public health measures to control the SARS-CoV-2 outbreak in Europe. We will develop and implement a plan for the dissemination and exploitation of results as part of WP1. As in all work in RECOVER we will align this plan with the existing dissemination and exploitation plans of PREPARE, VALUE-Dx and others where possible. The essentials of this plan are described below.

**Target groups**

Our dissemination and communication efforts will be targeted at the following stakeholders:

A. **Public health authorities and policy makers**: this includes WHO, ECDC, EU DG SANTE and national public health agencies, the European Medicines Agency;
B. **Health care professionals**: this includes general practitioners, nurses, clinicians and physicians at the frontline of patient care;
C. **Wider research community**: this includes other research projects and networks in Europe and beyond actively involved in the SARS-CoV-2 research response;
D. **Funders**: this includes the European Commission’s DG Research as the funder of RECOVER, GloPID-R, Wellcome, CEPI, IMI and others;
E. **Patients**: this includes the patients consulting Primary Care and hospitalized with SARS-CoV-2 as well as the persons at risk;
F. **Media**: this includes the general printed, web and audiovisual media as well as more specialised media.

Each group is heterogeneous in its information needs and roles in the SARS-CoV-2 outbreak response. For each group we will design and implement specific dissemination materials and platforms to ensure that the right information reaches the right users in a time-frame relevant to their roles and responsibilities in the SARS-CoV-2 response.

**Dissemination actions foreseen**

**Ad A: Public health authorities and policy makers**

We will share our (preliminary) results with this important group of stakeholders via regular policy briefs, summarizing our findings in a concise manner. The results of our clinical, laboratory and epidemiological modeling studies will feed into the public health policies regarding outbreak response interventions. Research evidence, collected during the outbreak, on the clinical spectrum of disease, on host- and pathogen-related determinants of severity, on the transmission dynamics, epidemic spread and on healthcare professional, patient and public perceptions will provide valuable supporting evidence for public health decision makers. Each policy brief will providing a snapshot overview of the results obtained thus far and their implications for public health interventions. These policy briefs will be sent out on behalf of all RECOVER research groups via direct channels of communication, where we will make sure that the information in each (updated) policy brief reflects the latest status of findings by RECOVER. Based on the combined professional networks with these stakeholders agencies we will develop a contact list with persons within these networks to whom the policy briefs should be sent out, respecting any internal communication processes within these organisations.

Upon request, RECOVER can elucidate (specific parts of) their research results presented in the policy briefs, in specific ad hoc policy meetings, working groups etc. Here, we can imagine this to be co-organised with other projects funded under this call topic. We will also leverage the existing advisory roles of some of the principal investigators involved in disseminating our findings with these organisations.
**Ad B Health care professionals**

The main information need at the level of this stakeholder group is the information from our clinical, laboratory and epidemiological modelling supporting more evidence based clinical decision-making during the outbreak, specifically in making well informed decisions about “is this particular patient at risk of developing severe SARS-CoV-2 respiratory syndrome or not?”, “where and under which containment measures should this patient be further treated” etc.

As with our dissemination to public health authorities we will provide regular updates to this stakeholder group in the form of healthcare briefs, where we outline out key findings and the implications for patient diagnosis and treatment, tailored to healthcare providers in primary care and hospital care. Here, we will make use of existing communication contacts within the primary care and hospital care networks active in PREPARE and VALUE-Dx, as well as at professional societies such as European Respiratory Society (ERS), European Society for Clinical Microbiology and Infectious Diseases (ESCMID), European Forum for Primary Care (EFPC), European Society for Intensive Care Medicine (ESICM) and others.

**Ad C Wider Research Community**

There is a wealth of other research response efforts being implemented by the wider European infectious diseases research response community. Many of our partners working in Europe, but also in regions outside of Europe (e.g. Africa and Asia) have informed us of their efforts and offered linking their efforts to those conducted in RECOVER.

For example, the Fondation Mérieux (FMER) of France, one of the colleague members of PREPARE in ISARIC informed us of the initiation of a multi-centre study on nosocomial transmission of the SARS-CoV-2 virus in South and South-East Asia and in Africa via the GABRIEL network in low income countries (LIC) (https://www.gabriel-network.org). Countries include Mali, Madagascar, Cambodia, India, Myanmar, Brazil; possibly Guinea, Burkina Faso and Niger. This study is similar to those proposed in Europe in RECOVER and aims to describe and document suspected or confirmed cases of nosocomial infections of SARS-CoV-2, their clinical spectrum and the determinants (risk factors / protection) at the participant hospitals. The FMER study will consist of: 1. A prospective, non-interventional - observational hospital-based study in adults and children of hospital departments, to assess SARS-CoV-2 cases and nosocomial transmission in the hospital, and describe infection prevention and control practices and policies; and 2. Capacity building and transfer of technology to rapidly develop and implement a RT-PCR in the member country laboratory and/or other laboratories. Data will be collected according to the operating modes of the various hospital services and their organization in terms of clinical or epidemiological research.

We will link with other studies outside of Europe such as these, through ISARIC where possible, exchanging protocols and information on research plans and results in support of a globally coordinated research response to the SARS-CoV-2 epidemic. We will make use of existing planned meetings of PREPARE, VALUE-Dx, ECRAID-PLAN, VEO, REACTinG, ISARIC and others to disseminate our findings to linked projects and networks globally.

Our clinical biology research in WP5 is aligned with similar studies ongoing in China, through partner 10 that serves one of the designated hospitals of the Chinese Academy of Sciences network, reserved for patients infected with the SARS-CoV-2. The WP5 cross-Europe collaboration, and the WP5-China interaction also will focus on bridging data generated in China with observations in Europe, through comparison of assays used, and exchange of assays standards.

**Ad D Funders**

This group of stakeholders is closely linked to the public health policymakers and includes major funders collaborating under GloPID-R (see www.glopid-r.org), CEPI, Wellcome and others. RECOVER’s principal investigators have direct contacts with these organisations, which we will leverage to establish direct lines of communication, informing them about key activities and (preliminary) results where this is requested.

**Ad E Patients**

Patients are the ultimate stakeholders of our proposed work. In our social science works in WP1, 2 and 3 we will engage into direct contact with patients, enabling us to incorporate the patient’ perspective in our work.
and in our communications outside of RECOVER. We will reach out to patient organisations such as the International Alliance of Patients’ Organisations (IAPO and European Lung Foundation (ELF) to assess their information needs and how we can best serve these out of RECOVER.

Ad F. Media
The international and national media (printed press, television, radio, news sites etc.) are in constant need of news on the development of the SARS-CoV-2 outbreak. Many of the investigators collaborating in RECOVER are being chased by media with requests for interviews and TV appearances on local, regional and international media, to provide expert insights and updates on the SARS-CoV-2 epidemic. As part of RECOVER, we do not have the intention to coordinate all these media appearances as this would not be feasible to organise in such a short time frame. We will though develop press releases at important time points and milestones in RECOVER 9e.g. decisions to go into Mode 3, decisions to upscale the clinical studies, important outputs etc.).

Management of Data
We will develop a Data Management Plan (DMP) based on the DMPS in PREPARE and VALUE-Dx. This RECOVER DMP will further detail the key elements as summarised below:

What types of data will the project generate/collection?
RECOVER will collect a range of clinical data (see WP1, WP2 and WP3), laboratory data (see WP4 and WP5) and epidemiological data (See WP6).

What standards will be used?
The WP2 and WP3 data will be collected using an eCRF within an Electronic Data Capture system. It is not anticipated that the initial set up of this data will match a predefined standard. Data will be stored in a central database and can be exported and processed for usage within the applicable work packages (e.g., WP2 and WP3) in any desirable format and standard. The requirements for data formats and standards will be defined during the development of the data management plan.

How will this data be exploited and/or shared/made accessible for verification and re-use? If data cannot be made available, explain why.
All clinical data collected within RECOVER will be deposited in a central repository, under the responsibility of partner 3. An online secure data portal for data sharing of this central repository will be developed and made accessible for the involved investigators to query, analyse and download final cleaned datasets. All data management tools and services will be GCP compliant where required and conform to the General Data Protection Regulation (GDPR). The costs for the data curation are covered by the project budgets.

How will this data be curated and preserved?
Curation of collected data will be defined in detail during the development of the data management plan in WP2 and WP3. In principle data captured related to the WP2 and WP3 study will be curated by the study sponsor. Processed data for specific analyses (e.g. social sciences studies) will be curated by the applicable WP. After data has been curated it will be integrated into a central repository under the responsibility of UMCU for preservation and future analysis.

How will the costs for data curation and preservation be covered?
Costs for data curation will be covered by the RECOVER funding requested.

Management of Knowledge
We will conclude a Consortium Agreement (CA) on the essential rights and obligations of the Beneficiaries in RECOVER. This CA will be based on existing CAs with the partners concerned, bringing the risk of lengthy legal negotiations to a minimum. The CA will include proper arrangements on the management of project data, ownership (including access to Background and Foreground, protection and ownership, transfer of ownership), in compliance with relevant articles in the Grant Agreement. The general principles and procedures underlying the exploitation and IP strategy of RECOVER will be included in the CA. Background
will be identified by the beneficiaries and will be included in the CA. As part of the RECOVER CA all beneficiaries will provide access to their Background knowledge to those beneficiaries that will need access for research purposes as part of RECOVER. The Foreground knowledge generated in RECOVER will be screened for exploitation potential by the WP (co-)leaders and will be protected in a timely fashion, to secure ownership of these results and rapid further uptake. Decisions to protect Foreground knowledge will be communicated without delay to the Governing Board as the responsible managerial body for the coordination of the Knowledge Management activities and monitoring compliance to the CA and the relevant articles in Grant Agreement (e.g. on Access to Background, Ownership, Protection and Exploitation of Results). In case of potential conflicts, the Governing Board will be consulted and asked for a final decision following CA procedures. At Beneficiary level the local Technology Transfer Offices, or equivalent organisational units with expertise in the legal aspects overall IP management, will be available to all key investigators in RECOVER.

COMMUNICATION ACTIVITIES

General principles
Our dissemination and exploitation strategy will be based on the following principles:

› All results will be shared openly as rapidly as possible to the relevant users;
› All communications out of will be centrally coordinated with all other networks to ensure coherency of (timing and content of) messaging across PREPARE, VALUE-Dx, COMBACTE and others;

Building on the communications processes of the PREPARE consortium, we will rapidly develop an impact and communications strategy for all research in the RECOVER consortium. The primary aim of the strategy is to ensure that research outcomes reach decision makers managing the public health or clinical response to SARS-CoV-2 in a timely way and in a format that is useful to them in conducting their role.

Objectives of the strategy are: (a) to build awareness of RECOVER research among the target ‘end user’ groups; (b) to identify mutual communication pathways at local, national and international levels and preferred communication products for target end users (e.g. policy brief); (c) to ensure that research findings are shared at the earliest point with these end user groups; (d) to track evidence of impact following from research findings.

To develop the impact strategy, we will identify target end user groups in consultation with the clinical research teams in WP2 and WP3. We will identify focal points in these end user groups, i.e. the person best positioned to rapidly disseminate research findings to a wider group. We will contact these focal points to share information about the research being planned and agree the most effective pathway for mutual sharing information. This pathway will be documented. The RECOVER communications team will then deliver the impact strategy and will be responsible for timely production of communication products such as single page policy briefs in multiple languages or infographics aimed at communicating research activity and results with European citizens. Once the emergency phase of the epidemic has passed, we will engage with our target end users through brief interviews or a stakeholder meeting to evaluate our activities in meeting their needs for rapid production of evidence to guide decision-making.

Visual identity
To design the visual identity for RECOVER, we will work with an external graphic design studio. The visual identity will include a logo as well as branded templates across Microsoft Office and Adobe suite. The logo will serve as the visual identity of RECOVER and perform as the means of being recognisable in order to create awareness, interest, and trust in the project. We will deliver the final brand guide which will be used across all communication channels including website, templates, presentations, and any other form of communication medium that RECOVER will use in the future. We will adhere to the following structural principles to develop RECOVER’s branding:

› Develop a simple and minimal design by using a clean and modern colour palette;
› Use a symbol expressing research and science but also the corporate character;
› Demonstrate the public health and societal benefits;

RECOVER Part B1-3

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Demonstrate the cross-border factor while showing the community of autonomous members working together.

**Online presence**
RECOVER will have its own online presence where information about the project will be available for interested stakeholders. The online presence will take form of a microsite or a landing page on one of the existing projects (e.g. PREPARE website). We will further create and manage social media accounts for RECOVER to disseminate project results, milestones and updates in a timely and digestible manner to key stakeholders and the general public.

**Publications**
Multiple journals have endorsed new open access policies for research related to SARS-CoV-2 and pre-print of papers that are under review by journals are available for rapid access to information. RECOVER’s research publications will not be placed under embargo and will be published in open access sources. Open access publishing means that an article is immediately provided in open access mode by the scientific publisher. In this way researchers can access and build on the findings of RECOVER without restriction.

**Communication outputs**
As a part of the communication dissemination plan for RECOVER, we will develop and disseminate a suite of collateral about the project and its progress. The collateral for the project may include:

- News updates;
- Policy briefs and healthcare briefs;
- Infographics;
- Brochures.

The aim of these products is to rapidly circulate key information in a format that is user friendly to decision makers managing the local, national and international response to SARS-CoV-2. In addition, these products will be designed to share information in a clear and de-jargonised way with European citizens. Our community advisory board is on standby to provide rapid input into the design of these products.
3. Implementation

3.1 Work Plan – Work packages and Project Planning

The work plan of RECOVER is organised into 6 Work Packages (WPs), as depicted in fig. 9. WP1 (not depicted in figure 9), involves the central management, dissemination and engagement activities in RECOVER. WP5B is the Chinese ‘counterpart’ of RECOVER WP5, funded through the State Basic Research Development Program of China (MOST), involving IP Shanghai.

All WPs will start immediately and will be closely aligned to ensure that intermediate results are quickly exchanged across the consortium.
Project Planning

The timelines below are indicative and will be adapted based on the evolution of the SARS-CoV-2 outbreak in Europe. RECOVER activities across the Work Packages will be implemented in three escalating Phases (see figure 3):

- **Phase 0**: this is the starting point of RECOVER. *Tasks marked with “0” will start right away and will continue upon completion of the task (in phase 1 and 2)*;
- **Phase I**: this is the phase that is entered into when the Governing Board decides to enter into Outbreak mode 3 (Research Response). *The start of tasks marked with “I” will depend on the timing of the decision by the Governing Board to enter into Mode 3 (Phase I)*;
- **Phase II**: this phase will be entered as per decision by the Governing Board in the event of widespread circulation of SARS-CoV-2 in Europe and marks the upscaling of the clinical studies to a larger group of sites/networks as described in section 1.3 and in the WP2 and WP3 tables. *The start of tasks marked with “II” will depend on the timing of the decision by the Governing Board to enter into Mode 3 (Phase II)*;

<table>
<thead>
<tr>
<th>Phase</th>
<th>WPs and tasks</th>
<th>Year 1</th>
<th>Year 2</th>
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<tbody>
<tr>
<td>0</td>
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<td>1 2 3 4 5 6 7 8 9 10 11</td>
<td>12 13 14 15 16 17 18 19 20 21 22 23 24</td>
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<td></td>
<td>WP 1 Management &amp; Impact</td>
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<tr>
<td>0</td>
<td>1.1 Consortium Coordination</td>
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<td>0</td>
<td>1.2 Dissemination and Communication</td>
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<td>0</td>
<td>1.3 Public survey</td>
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<td></td>
<td>WP2 Clinical Study Primary Care</td>
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<tr>
<td>0</td>
<td>2.1 protocol development</td>
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<td>0</td>
<td>2.2 EARL procedures</td>
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<td>0</td>
<td>2.3 Pt enrollment and data/sample collection</td>
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<tr>
<td>0</td>
<td>2.4 Data management</td>
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<td>0</td>
<td>2.5 HC/Pt survey</td>
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<td>WP3 Clinical Study Hospital Care</td>
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<tr>
<td>0</td>
<td>3.1 Facilitating uniform data collection of the first SARS-CoV-2 infected patients in Europe</td>
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<tr>
<td>0</td>
<td>3.2 Reactivation of MERMAIDS-ARI study sites</td>
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<tr>
<td>0</td>
<td>3.3 Protocol development</td>
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<tr>
<td>0</td>
<td>3.4 Selection of new study sites</td>
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<tr>
<td>0</td>
<td>3.5 EARL procedures</td>
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<tr>
<td>0</td>
<td>3.6 Data management</td>
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<tr>
<td>1, II</td>
<td>3.7 Conduct of MERMAIDS-ARI (phase I) and MERMAIDS-ARI2.0 (phase II)</td>
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<tr>
<td>Phase</td>
<td>WPs and tasks</td>
<td>Year 1</td>
<td>Year 2</td>
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<tr>
<td>I, II</td>
<td>3.8 Establish the spectrum of disease severity and outcomes</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>I, II</td>
<td>3.9 Quantify severe SARS-CoV-2 infections</td>
<td>3</td>
<td>4</td>
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<tr>
<td>I, II</td>
<td>3.10 Identify host risk factors</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>I, II</td>
<td>3.11 Supporting the REMAP-CAP Platform</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>I, II</td>
<td>3.11 Exploring opportunities of testing novel diagnostics for SARS-CoV-2</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>0</td>
<td>3.12 Rapid survey of health care professionals</td>
<td>11</td>
<td>12</td>
</tr>
</tbody>
</table>

**WP4 Lab. support services**

| 0 | 4.1 Lab. selection | 13 | 14 |
| 0 | 4.2 Dx deployment | 15 | 16 |
| 0 | 4.3 Development of SOPs | 17 | 18 |
| 0 | 4.4 EQA | 19 | 20 |
| 0 | 4.5 SOPs for sampling | 21 | 22 |
| 0 | 4.6 Etiologic diagnosis | 23 | 24 |
| 0 | 4.7 Correlation of viral load | |
| 0 | 4.8 Biobanking | |

**WP5A Clinical Biology**

| 0 | 5.1 Protocol preparation | |
| 0 | 5.2 Virus Characterisation | |
| 0 | 5.3 Role of prior CoV exposure | |
| I | 5.4 Host transcriptome characterisation | |
| II | 5.5 Virus evolution monitoring | |

**WP6 Epidemiology & Modeling**

| I | 6.1 Contact study | |
| I | 6.2 Household transmission study | |
| I | 6.3 Estimation of transmission parameters | |
| I | 6.4 Impact of social distancing measures | |
| I | 6.5 Importation risk monitoring | |
3.2 Management structure and procedures

For the implementation of RECOVER we will set up a project management structure as depicted in figure 10. This management structure is designed to facilitate quick and efficient exchange of information across the teams working at the Beneficiaries and quick decision-making concerning any adjustments needed in the workplans and budgets if needed. All participating institutes and their research groups, collaborating in RECOVER have ample experience in the managerial aspects of international collaborative research projects, including those funded through EU DG Research Frameworks projects. Their local organisational and financial support infrastructures and staff are trained and experienced in participating in H2020 proposals and as such are adequately equipped to provide their support to the principal investigators involved. In the following paragraphs we have set out the essential elements of the project management structure and processes, to be further detailed in the RECOVER Consortium Agreement.

RECOVER Governing Board (GB)
The GB is the managerial, coordinating epicenter of RECOVER. The GB consists of the lead representatives of all the Beneficiaries in RECOVER and is chaired by the Coordinator (Herman Goossens), with Sylvie van der Werf (IP) acting as vice-Chair. The GB is responsible for (i) ensuring the overall alignment of the activities across the WPs, (ii) monitoring the progress of the project activities towards the key milestones, (iii) the budget utilization per WP, (iv) the compliance with the publications policy and (iv) monitoring external events/risks that may need appropriate mitigation by RECOVER (together with the OMC, see below). GB Members are accountable for the performance of their respective Beneficiary’s
team(s) working in RECOVER. As such, the GB is responsible for taking the final decisions on any mitigative measures needed in response to (unforeseen) events and risks, that affect the composition of the Consortium, or any major deviations in the project’s activities and associated budgets. Examples are the addition of new Beneficiaries, or major changes in project roles and tasks and associated reallocations of budgets. GB decisions are made by means of voting with each Beneficiary having one vote and GB-decisions requiring a two-third majority. Specific procedures regarding voting and veto rights will be agreed upon in the RECOVER Consortium Agreement. The Coordinator, Herman Goossens is responsible for the formal communications to the European Commission on behalf of RECOVER.

RECOVER Scientific Committee (SC)
The SC is the scientific advisory body of RECOVER where all lead investigators from all WPs regularly come together to share and discuss intermediate results obtained, any obstacles encountered and the need for any adjustments based on these findings and the further development of the SARS-CoV-2 epidemic in Europe. The SC is Chaired by the Coordinator with the Scientific Coordinator acting as co-chair. It meets on a regular basis (at the start of the project at least every one to two weeks via TC to ensure that at any given time all lead investigators are well informed about the progress in the other WPs). Any contingency measures must be put forward by the SC to the GB for appropriate and timely decision making.

The table below shows the composition of the SC, with the persons mentioned in italics and marked with * serving on the Governing Board of RECOVER. Lead investigators from Partner 10 IPS active in WP5B will be represented via Marion Koopmans, acting as the WP5-WP5B liaison and will be invited to participate in SC teleconferences when possible.

<table>
<thead>
<tr>
<th>WP</th>
<th>RECOVER SC (italic * = also Governing Board Member)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WP1 (Mgt and Impact)</td>
<td>Herman Goossens* (WP1 Lead), Sylvie Van der Werf (WP1 Co-Lead), Tamara Giles Vernick (IP); Nina Gobat (UOXF)</td>
</tr>
<tr>
<td>WP2 (Clinical studies PC)</td>
<td>Chris Butler* (WP2 Lead), Emily Bongard, Nina Gobat, Sarah Tonkin-Crine (UOXF); Alike van der Velden (WP2 co-lead), Theo Verheij (UMCU); Sibyl Anthierens (UA)</td>
</tr>
<tr>
<td>WP3 (Clinical Studies HC)</td>
<td>Marc Bonten (WP3 Lead)<em>, Patricia Bruining, Lennie Derde (UMCU); Peter Horby</em> (WP3 co-lead), James Lee, Nina Gobat, Sarah Tonkin-Crine (UOXF); Sibyl Anthierens (UA); Carlo Giaquinto* (PENTA), France Mentré (INSERM)</td>
</tr>
<tr>
<td>WP4 (Lab. support services)</td>
<td>Greet Ieven (WP4 Lead), Veerle Matheeussen (UA); Menno de Jong (AMC) (WP4 co-lead)</td>
</tr>
<tr>
<td>WP5 (Clinical biology)</td>
<td>Marion Koopmans* (WP5 Lead), Bart Haagmans, (Erasmus MC); Christian Drosten* (WP5 co-lead), Victor Corman (Charité); Sylvie Van der Werf* (IP) Menno de Jong (AMC)*</td>
</tr>
<tr>
<td>WP6 (Transmission, epidemiology and modeling)</td>
<td>Yazdan Yazdanpanah*, Vittoria Colizza, Xavier Duval (INSERM) (WP6 lead); Simon Cauchemez (IP) (WP6 co-lead); Patricia Bruining (UMCU)</td>
</tr>
</tbody>
</table>

RECOVER Outbreak Mode Committee
If RECOVER is funded, the acting Outbreak Mode Committee of PREPARE set up specifically in PREPARE for the SARS-CoV-2 outbreak will be replaced by the RECOVER GB. As such, in consultation with the SC members, the GB will act as the central decision-making unit in RECOVER, deciding on escalation of the Outbreak Response Mode from the current Mode 2 to Mode 3, triggering the initiation of the upscaled clinical research responses.

RECOVER WP Teams
At the operational level, WP teams will be set up, responsible for executing the WP tasks as described in section 1.3. In the compositions of these WP teams we will build on the established operational teams at the Beneficiaries. The WP teams will be operationally coordinated by their representatives in the Scientific Committee.
RECOVER Project Office

The RECOVER Project Office will be composed of a Project Manager, a Project secretary and a Financial Officer, stationed at the UA. Here, we will leverage the fully operational support infrastructure active for PREPARE and VALUE-Dx, enabling us to realise cost-efficiencies and only allocated a limited budget to the administrative coordination of RECOVER.

In the RECOVER Project Office the Communication officers active in PREPARE, VALUE-Dx and ECRAID-Plan will be responsible for coordinating the external communications of RECOVER. This way, we can ensure that they will align their communications regarding RECOVER and those related to the SARS-CoV-2 outbreak in general with their counterpart communication teams/officers of COMBACTE, PENTA, REACTing, COMPARE/VEO and ISARIC. By connecting the communication team across these networks we aim to align the timing and content across the messages coming out of all networks in relation to RECOVER.

Progress reporting and monitoring

The first months of RECOVER will be decisive in terms of realizing our full potential to have an impact on clinical and public health interventions in the context of the SARS-CoV-2 outbreak in Europe. We will therefore continue to organise weekly – and if necessary daily – teleconferences with the Scientific Committee in which all WP leads and co-leads report their progress of work across the various research tasks and exchange relevant information across RECOVER. In addition, we will set up a quick document repository where we can quickly exchange working documents, protocols etc. internally. We are in the process of determining which existing IT tools used by the networks involved are best fitted in terms of feasibility and security. The Project Office will document and keep track of all major action points, decision and progress of work on milestones and deliverables to create regular snapshot updates of the work across all WPs and circulate these amongst the SC so that each research group is aware of where the other research groups are in terms of their tasks and deliverables.

Complementary to this quick and researcher-friendly progress monitoring process we will organize face-to-face meetings with the GB/SC in parallel to already planned meetings of PREPARE/VALUE-Dx and/or ECRAID-Plan. Each WP is to keep track of, and document the progress of work per task and associated deliverables and milestones. The Project office will develop a simple user friendly template for such a ‘living’ WP progress report that can rapidly be processed into reports to the European Commission and serve as the basis for external communications via the RECOVER Communications team.

The SARS-CoV-2 outbreak research response is inherently done under great uncertainties, with new data and information rapidly coming available on a daily basis. The primary uncertainty, with large impact on RECOVER is if, where and when the SARS-CoV-2 outbreak becomes widespread in Europe. This would trigger RECOVER to initiate the Phase II of our clinical research studies, (see section 1.3) and WPs 5 and 6 to perform parts of their tasks of relevance in widespread circulation scenarios. All investigators in RECOVER are well embedded in the European and global field on emerging outbreak preparedness and response and as such are well-positioned to have direct and rapid access to information needed for the RECOVER outbreak Mode Committee (=GB) to trigger the Outbreak Mode 3 in RECOVER.

In addition to the uncertainties surrounding the development of the SARS-CoV-2 outbreak, there are many barriers that hamper the rapid initiation of clinical research in response to emerging ID outbreaks. PREPARE introduced the term “EARL” barriers as the complex, interrelated set of Ethical, Administrative, Regulatory and Logistical requirements that act as all ‘non-technological’ and ‘non-scientific’ delaying factors in clinical research in the context of epidemics, and has experience in minimising their impact.
3.3 Consortium as a whole

RECOVER involves key partners from PREPARE – Partners 1 (UA), 3 (UMCU), 4 (UOXF), 5 (Erasmus MC), 6 (Charité), 8 (AMC), and 9 (PENTA) –, augmented with specific specialised research groups from partner 2 (IP) and 7 (INSERM) and linked to SARS-CoV-2 research response efforts conducted by IPS in China.

This rapidly built consortium is specifically designed to tackle the most pressing research questions that need to be addressed in support of improved patient and population-level interventions to control the impact of the SARS-CoV-2 outbreak on Europe and European citizens. It is testament to the research preparedness and response capacity of all networks involved to put together, under great time constraints, a focused research response proposal that truly builds on the expertise and research infrastructures of leading European centres of excellence on:

› Infectious diseases clinical research; With UA, UMCU, UOXF, and PENTA RECOVER has the coordinating centres of the PREPARE and VALUE-Dx clinical research studies on infectious diseases in acute respiratory infections, enabling RECOVER to rapidly initiate patient enrolment in primary and hospital care centres across Europe, should the SARS-CoV-2 Epidemic reach Europe.

› Advanced clinical biology studies on Coronaviruses; RECOVER includes the three EU reference laboratories in the WHO global response network for SARS-CoV-2 (Erasmus MC, Charité and IP), built on their expertise gathered through COMPARE, HONOURS, EVD-LabNet, REACTING and ZAPI.

› Epidemiological modelling of infectious diseases research; RECOVER includes the European top infectious disease modelling groups from IP and INSERM;

› Social sciences aspects of infectious diseases outbreak response; RECOVER includes European lead social scientists from IP (the Coordinator of the SONAR-Global social sciences network on infectious diseases), UOXF, UA and UMCU;

For a more detailed overview of the lead investigators and their expertise involved, we refer to section 4.1.

Through these nine partners involved, RECOVER has direct links with key (EU/IMI funded) networks in Europe, focusing on various interrelated activities in infectious diseases research preparedness and response (see fig. 11). For a description of these networks, we refer to section 4.

This puts RECOVER in the unique position to connect its research efforts to and exchange research results, protocols etc. with, these networks.

Moreover, it puts RECOVER in the unique position to leverage these networks acting as gateways to the wider clinical and public health actors, in rapidly and coherently disseminating our research results to clinical and public health decision makers and policy makers.

![Fig. 11: Summary overview of the Beneficiaries and directly linked networks and projects in RECOVER](image-url)
3.4 Resources to be committed

For the implementation of RECOVER we request an EC contribution of EUR 4,995,820 Euros. The Governing Board of RECOVER will continue to follow closely the developments in Europe concerning the SARS-CoV-2 epidemic and will continuously review the allocated budgets per work package to ensure that available funds are prioritised to those research tasks that are needed to address the most urgent questions, based on how the SARS-CoV-2 epidemic evolves in Europe. The budgets allocated to the tasks in WP2 Clinical study Primary Care and WP3 Clinical Study Hospital Care – for Phase I as well as for Phase II – are subject to decision making by the RECOVER Governing Board to enter into Mode 3- triggering Phase I, and to go into Phase II. Where possible, and in consultation with the European Commission, funding available in PREPARE until 31/1/2021 will be leveraged to support research tasks in RECOVER.

Table 3.4b: ‘Other direct cost’ items (travel, equipment, other goods and services, large research infrastructure)

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<tr>
<th></th>
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<th>Cost (€)</th>
<th>Justification</th>
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<td>1. UA</td>
<td>Travel</td>
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<tr>
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<td>Other goods and services</td>
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<td>Other goods and services</td>
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<td>Cost (€)</td>
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*Note: at this stage, we do not envisage to claim costs for travel and equipment in this project.*

3.4c: Other sources of funding for the tasks described in the Description of the Action (DoA) and covered by this H2020 grant.

No funding from any other third party for the tasks described in the Description of Action has been received at the time of grant agreement preparation. In the event that this changes during the implementation of the action, the consortium will inform the Commission services.

3.4d: Other sources of funding for any complementary tasks closely related to the work covered by this H2020 grant.

No funding from any other third party for any complementary tasks closely related to the work covered by this grant has been received at the time of grant agreement preparation. In the event that this changes during the implementation of the action, the consortium will inform the Commission grant services.
References

1 Munster et al. NEJM 2020


3 https://doi.org/10.1016/S1473-3099(13)70327-X; https://isaric.tghn.org/CCP/


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Lavielle M. Mixed effects models for the population approach: models, tasks, methods and tools. CRC press; 2014.

9 https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.4.2000057
4. MEMBERS OF THE CONSORTIUM

4.1 Participants

PARTNER 1: UNIVERSITY OF ANTWERP (UA)
PARTNER 2: INSTITUT PASTEUR (IP)
PARTNER 3: UNIVERSITY MEDICAL CENTRE UTRECHT (UMCU)
PARTNER 4: ERASMUS UNIVERSITY MEDICAL CENTER (ERASMUS MC)
PARTNER 5: UNIVERSITY OF OXFORD (UOXF)
PARTNER 6: CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN (CHARITÉ)
PARTNER 7: INSTITUT NATIONAL DE LA SANTÉ ET DE LA RECHERCHE MÉDICALE (INSERM)
PARTNER 8: ACADEMIC MEDICAL CENTER (AMC)
PARTNER 9: FONDAZIONE PENTA (PENTA)
PARTNER 10: INSTITUT PASTEUR SHANGHAI (IPS)

4.2 Third parties involved in the project (including the use of third party resources)

5. ETHICS AND SECURITY

5.1 Ethics

5.2 Security

6. DATA SHARING
4. MEMBERS OF THE CONSORTIUM

4.1 Participants (applicants)

PARTNER 1: UNIVERSITY OF ANTWERP (UA)

Description of participant and main tasks

The University of Antwerp (UA) ranks amongst Europe's leading universities in terms of relative scientific impact scores in the natural and biomedical sciences (EU Science and Technology Indicators for 2003). The Laboratory of Medical Microbiology (LMM) is part of the Vaccine & Infectious Disease Institute at UA and has an international reputation in investigating the impact of antibiotic use and emergence of antimicrobial resistance both at the ecologic and individual level, the latter by utilizing state-of-the-art molecular techniques as well as developing molecular diagnostic tests for clinical applications. LMM is also one of two central labs involved in an European public health initiative aiming to set up a database of whole genome maps of bacterial pathogens causing outbreaks. The LMM is the coordinator of PREPARE (Platform for European Preparedness against (Re-)emerging Epidemics), ND4ID (New Diagnostics for Infectious Diseases), VALUE-Dx and partner in COMBACTE, ECRAID-Plan andCOMPARE.

Profiles of main persons involved

Prof. dr. Herman Goossens (m): Herman Goossens is head of LMM, both at the UA and the Antwerp University Hospital (UZA), director of Diagnostic Laboratory of Clinical Biology at UZA and has a part-time position at the UMC Utrecht. He is an authority on antibiotic use, resistance and molecular diagnostics and has published his research in over 600 full papers in peer-reviewed scientific journals. He is the coordinator of several European projects, including PREPARE (Platform for European Preparedness Against (Re-)emerging Epidemics, ECRAID-Plan (European Clinical Research Alliance for Infectious Diseases), VALUE-Dx (Value of diagnostics to combat antimicrobial resistance by optimizing antibiotic use), and ND4ID (New Diagnostics for Infectious Diseases), and leads the COMBACTE-NET WP3 on “Establishment, Training, and Maintenance of a Laboratory Surveillance Network” (LAB-Net). He was also the coordinator of ESAC (European Surveillance of Antimicrobial Consumption), GRACE (Genomics to Combat Resistance against Antibiotics in Community-acquired LRTI in Europe), RAPP-ID (Development of Rapid Point-of-Care test Platforms for Infectious Diseases) and participated in several other EC projects (ROUTINE, R-GNOSIS, SATURN, APRES, ARPEC, RESCUE). His professional goal is to bridge the gap between basic and clinical research, to enhance the standard of healthcare, public health and professional standards, for the good of the public in large. His vision is to build a sustainable infrastructure for clinical research on infectious diseases in Europe.

Prof. dr. Greet Leven (f): PhD, is professor at the faculty of medicine and was chief of laboratory of medical microbiology at University hospital until August 2016. She has long standing experience with the development and implementation of both conventional and molecular diagnostic tests in the clinical microbiology laboratory. Her main field of interest is diagnosis of respiratory infections. She has published her research in over 200 full papers in peer-reviewed scientific journals and chapters in 10 books. She has been the Work package leader for bacterial genomics in the EC funded FP6 project GRACE and the WP leader for the PREDICT diagnostics work package in PREPARE. She holds several expert positions in Belgium, was President of the European Study Group on Molecular Diagnostics of ESCMID from 2000-2010 and is Scientific Advisory member of QCMD (Quality Control of Molecular Diagnostics).

Prof. dr. Samuel Coenen (m): Samuel Coenen (ORCID 0000-0002-1238-8052) is professor clinical epidemiology in the Department of Epidemiology and Social Medicine at UA, former head of the Centre for General Practice and vice-chair of the Department of Primary and Interdisciplinary Care (ELIZA), coordinating its infectious disease unit and its primary care research network (PCN), and collaborating closely with LMM. His research focuses on the multidisciplinary study of infectious diseases, particularly on the management of (lower) respiratory tract infections in primary care in the context of antimicrobial resistance and is published in over 140 full papers in peer-reviewed...
Prof. Sibyl Anthierens (f): Sibyl Anthierens is a social scientist at the department of Primary and Interdisciplinary Care (ELIZA) and collaborates closely with LMM. She is also the co-director of QUALUA (Qualitative Health Research University of Antwerp). Her research reflects the complexity of the health care system and aims at understanding how it works taking context into account. It is clear that evidence alone is not enough to be implemented and that elements of context play a crucial role in translation and adoption of evidence, management strategies or the way that care is delivered. All her areas of application involve drawing together a set of qualitative research methodologies and the so called "mixed methods". She has been co task-lead in close collaboration with UOxford social science team in several European projects: e.g. Value-DX (a European Public-Private Partnership to fight antimicrobial resistance through diagnostics), GRACE (Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe: www.grace-lrti.org), CHAMP (Changing Health care behavior of professionals and the general public towards a more prudent use of anti-microbial agents) and PREPARE (Platform for European Preparedness against (re) emerging epidemics).

Dr. Veerle Matheeussen (f): Veerle Matheeussen (PhD) is a medical microbiologist at the clinical microbiology laboratory of the University Hospital of Antwerp (UZA) and researcher at the Laboratory of Microbiology at UA. She is involved in the diagnostics work package of PREPARE, focusing on molecular detection of respiratory viruses.

Selection of relevant publications


List of relevant projects

PREPARE: www.prepare-europe.eu

The Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE) is a large scale European project, including 27 beneficiaries and is funded by the EU FP7 Programme. PREPARE aims for the creation of operational readiness for rapid deployment of harmonised European clinical studies for any infectious disease outbreak and effective spread of evidence-based clinical guidelines via public health agencies to healthcare centres over the globe. To date, 5 trials are being managed and most of these trials are using the CLIN-NET and LAB-NET infrastructure of COMBACTE.
COMBACTE: [www.combacte.eu](http://www.combacte.eu)

COMBACTE (Combatting Bacterial Resistance in Europe) is part of the IMI funded programme ND4BB (New Drugs for Bad Bugs) and focuses on improving the clinical development of antibiotics. The COMBACTE programme includes four consortia: COMBACTE-Net, COMBACTE-Care, COMBACTE-Magnet and COMBACTE-CDI. The goals are to create a self-sustaining antibacterial clinical trial network and to increase the efficiency of antimicrobial drug development. To this purpose, it has established an infrastructure consisting of four high-quality networks: CLIN-NET, LAB-NET, STAT-NET and EPI-NET. By February 2020, COMBACTE LAB-Net is active in 41 European countries, with a total of over 800 laboratories.

VALUE-Dx: [https://value-dx.eu](https://value-dx.eu)

VALUE-Dx (Value of diagnostics to combat antimicrobial resistance by optimizing antibiotic use) is the Innovative Medicines Initiative (IMI) project that brings together in vitro diagnostic companies and non-industry partners to combat antimicrobial resistance (AMR) and improve patient outcomes. To help build the medical and economic case for rapid diagnostics in the fight against antibiotic resistance, VALUE-Dx will establish a sustainable European Standardised Care Network which is adequately trained and resourced to conduct clinical trials. Currently, VALUE-Dx is conducting a point prevalence audit survey (PPAS) in 18 European countries to record information about patients who seek healthcare for community acquired acute respiratory tract infections (CA-ARTI), helping researchers to benchmark patterns of testing and antibiotic prescribing. Two clinical studies, to be conducted in the next winter seasons, are being designed to demonstrate the value of diagnostics in the optimal management of CA-ARTI in different European healthcare settings.

ECRAID-Plan: [www.ecraid.eu](http://www.ecraid.eu)

Building on the foundations of the European consortia COMBACTE and PREPARE, ECRAID aims to advance clinical research in the field of infectious disease by further organizing and developing a European clinical research network. The network will function as the backbone of clinical research activities, providing an efficient infrastructure capable to perform all clinical trial aspects, from study design to scientific publication. All activities will be coordinated by a lean, centralized organization allowing easy access for all relevant stakeholders. The current ECRAID-Plan project is a two-year project (January 2019-Dec 2020) that will develop the business plan for ECRAID. ECRAID is aiming to launch its operations by the end of 2020.

COMPARE: [www.compare-europe.eu](http://www.compare-europe.eu)

The COllaborative Management Platform for detection and Analyses of (Re-) emerging and foodborne outbreaks in Europe (COMPARE) is an EU H2020 funded project, coordinated by DTU. COMPARE is a multidisciplinary research network that is set up with the common vision to become the enabling analytical framework and globally linked data and information sharing platform system for the rapid identification, containment and mitigation of emerging infectious diseases and foodborne outbreaks. The system sets out to integrate state-of-the-art strategies, tools, technologies and methods for collecting, processing and analysing sequence-based pathogen data in combination with associated (clinical, epidemiological and other) data, for the generation of actionable information to relevant authorities and other users in the human health, animal health and food safety domains.

ND4ID: [http://www.nd4id.eu](http://www.nd4id.eu)/

There is a large unmet clinical need for more rapid point of care (POC) in vitro diagnostics IVDs generating more clinically relevant, actionable information, requiring a change in the current approach in training researchers on IVDs, generating a new ‘breed’ of IVD researchers capable of closing the gap between the clinical and technological perspective. ND4ID is a H2020 funded project coordinated by the University of Antwerp and takes up this challenge by offering 15 ESRs a world-class first of its kind training programme where they will be exposed to the full breadth of disciplines spanning clinical, technological and market-oriented viewpoints, from both the academic and non-academic sector. Through a set of synergistic research projects on novel POC assays, targeting the most important and urgent clinical needs at world leading academic or private sector research groups, the ESRs are offered a holistic training program, preparing them to be lead players in the future IVD field. This training through research is augmented by a unique comprehensive network-wide training programme covering clinical, technical and translational knowledge and skills of relevance to IVD research, development and exploitation. As such, ND4ID will
deliver ESRs that will be in high demand serving as an example for other academic and non-academic actors active in training IVD researchers and further strengthening Europe’s position in the internally competitive arena of IVD technology.

**Description of significant infrastructure, relevant to RECOVER**

All infrastructure and personnel required to carry out the proposed work is available at the L2 laboratory of LMM, including standard microbiological equipment, several PCR and qPCR devices, high-throughput sample processing, ELISA multiplate readers, Roche gel scanners, RT-PCR (Roche) equipment, etc., necessary to support the multitiered nature of the research proposed in WP4. For NGS, LMM has an expanded platform that includes 2 Illumina MiSeq machines, an Oxford Nanopore, and a recently acquired long-read PacBio-Sequel II sequencer. We also have a robotics platform for high throughput sample handling and library preparation as well as basic equipment for NGS (gel electrophoresis + camera system, nanodrop, qubit, bioanalyzer). In addition, we have well-trained bioinformaticians who have developed simple, user-friendly NGS analysis pipelines and will take up the data analysis. Thus, the UA research network has gathered all relevant competences within the different expertise areas, microbiology, metagenomics, and clinics, which are essential for the multidisciplinary nature of the project.

To fulfill task WP4.9 LMM has a fully functional biobank (called the UA-UZA biobanking facility) which consists of a central facility of over 30 freezers coupled to local hubs, one of which is stationed at LMM. The LMM hub consists of fourteen -80°C freezers and one -180°C liquid nitrogen vessel, all temperature monitored and connected to an alert and CO2 back-up system. The entire biobank is governed using a SLIMS system documenting all sampling handling and a list of key sample data and is connected to a local database containing all scientific data.
PARTNER 2: INSTITUT PASTEUR (IP)

Description of participant and main tasks

The Institut Pasteur is a private, state-approved non-profit foundation for biomedical research, established in 1887 by Louis Pasteur and hosting some 2,400 people (scientists, engineers, technicians and administrative staff) of over 60 nationalities. Its mission is built upon three cornerstones: 1/ Research: 11 research departments divided into 130 research units bringing together multidisciplinary teams of scientists work at the very forefront of infectious diseases research, and are also dedicated to immunology, molecular biology, neurosciences, development biology, stem cells, genetics and genomics. 2/ Teaching: The Institut Pasteur Teaching Centre offers 27 courses attended each year by about 500 students from all over the world and is also a training centre for young scientists (Master or PhD fellows). Courses cover three main areas of study: Mechanisms of living organisms, Biology of microorganisms and Epidemiology and Public Health. 3/ Public Health: The Institut Pasteur’s public health mission is to promote the transfer of scientific discoveries made in its research laboratories to human health applications. It is actively involved in clinical research projects aimed at developing innovative therapies. As a microbiological observatory for communicable diseases, Institut Pasteur coordinates epidemiological surveillance of diseases throughout France via the 15 National Reference Centres (CNR) hosted by its laboratories. These centres support health authorities in the areas of diagnosis, epidemiological surveillance, and research. Of the 15 centres, seven are also World Health Organization Collaborating Centres (WHOCCs) tasked with the same duties in the international arena. The Institut Pasteur is also at the centre of a unique international network of 32 institutes, stretching across all five continents and all affiliated in partnerships.

Profiles of main persons involved

Prof. dr. Sylvie van der Werf (f):

Prof. Sylvie van der Werf is the head of the Virology department, of the National Reference Center on Influenza Virus and of the Molecular Genetics Laboratory research unit at Institut Pasteur. In the context of her Public Health responsibilities, since 1995, she was involved in various major virus emergence events. In 2003, as one of the WHO SARS reference laboratories, she contributed to the determination of the etiology of SARS and characterization of sites of virus shedding and kinetics of virus excretion. From 2004 on, following the reemergence of H5N1 viruses in South-East Asia, as WHO H5 reference laboratory, she contributed to the characterization of the H5N1 viruses’ genetic and antigenic evolution, in collaboration with Institutes from the International network of Institut Pasteur, notably with P. Buchy (Institut Pasteur, Cambodia). In 2009, she was at the heart of the surveillance of the 2009 H1N1 pandemic in France and contributed to the description of the kinetics of virus excretion and analysis of determinants of severity in collaboration with colleagues for various hospitals in Paris. More recently, she was mobilized with the emergence the Middle-East Respiratory Syndrome coronavirus (MERS-CoV). With her team, she detected and investigated two cases of infection by the MERS-CoV in France in 2013 documenting human-to-human transmission and providing information about the excretion patterns of this new virus. Prof. Sylvie van der Werf also contributed to several other EU funded projects such as EVAg, EVA-GLOBAL and PREPARE. Prof. Sylvie van der Werf was also the former coordinator of the FP7 PREDEMICs project.

Dr Tamara Giles-Vernick (f),

Dr Tamara Giles Vernick, Director of Research, is the first leader of a social sciences research unit (Anthropology and Ecology of Disease Emergence) at the Institut Pasteur in its 120-year history. A medical anthropologist and historian specializing in processes of disease emergence and in global health, she has directed large, multi-centred projects in Africa and trained social scientists, public health and medical professionals in Africa, the Middle East, southeast Asia, North America and Europe. Since 2009, she has collaborated closely in research and interventions with epidemiologists, virologists, microbiologists on emerging diseases and vaccination in LMICs. As the Social Sciences Leader on a large institutional programme, Inception, held by the Institut Pasteur, she is responsible for coordinating French social sciences partners in research and response to problems of emergence. She is the Coordinator of the SONAR-Global network, the H2020 funded international network of social sciences research centres to help address governance and other challenges in the preparedness for and the response to infectious
threats.

**Dr. Simon Cauchemez (m) Mathematical Modelling of Infectious Diseases Unit**

Dr Cauchemez is specialized in the development of state-of-the-art statistical and mathematical methods to address infectious threats, with the aim to increase the understanding of how pathogens spread in populations, assess the impact of interventions, support policy making and optimize control strategies. During his career, he has been involved in real-time risk assessments and support to policy making during a number of major emerging or re-emerging infectious disease epidemics including the H1N1pdm09 pandemic influenza in 2009, MERS-CoV in the Middle East, Ebola in West Africa in 2013-2014, the emergence of Zika in the Americas and a large plague epidemic in Madagascar in 2017. His work is based on the analysis of a broad range of data collected in the field including epidemiological and virological surveillance, transmission studies, outbreak investigations, clinical and laboratory data, serological data, environmental and climatic data. He has co-authored 134 publications, with more than 7,000 citations, an h-index of 38 (Web of Science 10 Feb 2020) including first or last author publications in Nature, Science, NEJM, Lancet, PNAS, Lancet ID, PLoS Med. He works closely with public health agencies in France and abroad to ensure his assessments can inform the public health response to epidemics.

**Prof. Marc Eloit (m),**

Prof. Marc Eloit is Professor of Virology and the former head of the Virology Unit at the Veterinary School of Maisons-Alfort. He is currently the head of the Pathogen Discovery laboratory at Institut Pasteur Paris and is searching for new or unexpected pathogens in patients of unknown etiology, including in China and South East Asia. His laboratory has been using for ten years Next Generation Sequencing as a key method for uncovering pathogens in human patients, animal reservoirs like bats and arthropods. He also routinely develops high throughput antibody screening tests for these novel viruses to detect spillovers events in contact populations. He has coordinated several multinational programs or workpackages, has worked as an expert or Committee chairman for French and European medical agencies and has published more than 130 publications ([https://www.ncbi.nlm.nih.gov/myncbi/1xKTWotCzv5Qn/bibliography/public/](https://www.ncbi.nlm.nih.gov/myncbi/1xKTWotCzv5Qn/bibliography/public/))

**Dr Hugo Mouquet (m),**

Dr. Hugo Mouquet is a molecular immunologist, head of the laboratory of Humoral Immunology at the Institut Pasteur. His research focuses on the humoral responses to human pathogens with a focus on HIV-1, Hepatitis viruses and emerging infections, and a dual interest in basic and translational research. His lab makes use of efficient methodological approaches to generate and characterize virus-specific human monoclonal antibodies. Using single B-cell capture and antibody expression cloning technics, his lab already identified dozens of potent cross-neutralizing human monoclonals against HIV-1, Chikungunya virus, Hepatitis B and E virus. He is the author of more than 65 papers in peer-reviewed journals (h index of 32). His research was supported by an ERC starting grant award for investigating human antibody responses to viruses (ERC-2013-StG 337146-HumAntiViruses).

**Dr. Etienne Simon-Loriere (m),**

Dr. Simon-Loriere is a group leader in the Virology department of Institut Pasteur. With a background in both experimental and computational biology, his main field of research is the study of RNA virus evolution, transmission and emergence, mainly using genomics. In particular, his work aims to better characterize features of RNA viruses which contribute to their success at expanding their host range or spread in human populations. His past work made important contributions to our understanding of the spread and adaptation of Ebolavirus strains in humans during the 2014 outbreak, or the link between features of immune responses and the severity of dengue virus infection.

**Dr. Pierre Charneau (m),**

Dr. Pierre Charneau is head of the molecular virology and vaccinology unit at Institut Pasteur and an acknowledged specialist of HIV, lentiviral gene transfer vectors and their medical applications. His discovery of the central DNA-flap structure in the HIV genome, and its role in viral entry into the nucleus of the infected cell, grounded the optimization of lentiviral vectors and paved the way to more than 20 years of development in gene therapy and vaccines based on this gene delivery technology. Charneau has published more than 100 research articles and holds 25 patents in the field of HIV and lentiviral vectors.
Selection of relevant publications


List of relevant projects


**EVA-GLOBAL**, Partner, Horizon 2020, European Commission (2020-2023)


**PREPARE**, Partner, Seventh Framework Programme, European Commission
PARTNER 3: UNIVERSITY MEDICAL CENTRE UTRECHT (UMCU)

Description of participant and main tasks

The UMC Utrecht is an internationally renowned research and teaching hospital with 1,200 beds and all medical specialties represented. Within the Department of Medical Microbiology and the “Julius Centre for Health Sciences and Primary Care” >50 researchers from different medical specialties collaborate in studying antibiotic resistance, epidemiology of infectious diseases and ICU-acquired infections, applying molecular, microbiological, epidemiological and theoretical methods. Both departments harbour extensive experience with large-scale multi-centre intervention trials and epidemiological analyses of large patient databases. UMCU is the Coordinator of 4 COMBACTE projects and leads the WP on the hospital-based REMAP-CAP study in PREPARE. In RECOVER it will be involved in the design and execution of the clinical studies.

Profiles of main persons involved

Prof. dr. Marc Bonten (m): Marc is professor of molecular epidemiology of infectious diseases, head of the department of Medical Microbiology and head of Infectious Disease research within the Julius Centre for Health Sciences and Primary Care. He has extensive experience in large-scale multi-centre intervention trials and epidemiological analyses of large patient databases in ICUs and antibiotic resistance. He is the scientific leader of COMBACTE and coordinator of the EC-funded Integrated Project R-GNOSIS. He has published >600 papers in peer-reviewed scientific journals and was associate editor of Intensive Care Medicine.

Dr. Patricia Bruijning (f): Dr. Bruijning-Verhagen is a Pediatrician and Associate Professor in infectious Diseases Epidemiology at the Julius Center for Health Sciences and Primary Care. Her epidemiological research focuses on characterizing and quantifying clinical disease and transmission of vaccine preventable and emerging infections to guide public health interventions. She coordinated a large multicenter clinical study on acute rotavirus hospitalizations and immunization in children and studied household transmission funded by a personal VENI (NWO) career grant. She has a key interest in community surveillance through the application of mHealth technology. She developed a methodology that has been successfully applied in several community (transmission) studies on respiratory, gastrointestinal and more recently, arbovirus infections in several (inter)national projects she collaborates in (OneHealth-PACT, SAFARI trial, ZleKA Monitor, ZIKAction)

Dr. Alike van der Velden (f): Alike is Assistant Professor at the Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, the Netherlands. She conducted, supervised and collaborated in several successful intervention trials in the Netherlands and in Europe to enhance prudent use of antibiotics in primary care. She was part of the core team having designed, organized and analyzed the ALIC4E trial in PREPARE and coordinated the 18 countries European primary care research network. She has the same role in the VALUE-Dx consortium in delivering the primary care studies.

Selection of relevant publications


List of relevant projects

**COMBACTE: [www.combacte.eu](http://www.combacte.eu)**

COMBACTE (Combatting Bacterial Resistance in Europe) is part of the IMI funded programme ND4BB (New Drugs for Bad Bugs) and focuses on improving the clinical development of antibiotics. The COMBACTE program includes three consortia: COMBACTE-Net, COMBACTE-Care and COMBACTE-Magnet. The goals are to create a self-sustaining antibacterial clinical trial network and to increase the efficiency of antimicrobial drug development. To this purpose, it has established an infrastructure consisting of four high-quality networks: CLIN-NET, LAB-NET, STAT-NET and EPI-NET. By February 2020, COMBACTE is active in 42 European countries, with a total of over 800 clinical sites and more than 500 laboratories. To date, 17 trials are being managed, including phase I – III trials for 6 new compounds against multi-resistant bacteria.

**PREPARE: [www.prepare-europe.eu](http://www.prepare-europe.eu)**

The Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE) is a large scale European project, including 27 beneficiaries and is funded by the EU FP7 Programme. PREPARE aims for the creation of operational readiness for rapid deployment of harmonised European clinical studies for any infectious disease outbreak and effective spread of evidence-based clinical guidelines via public health agencies to healthcare centres over the globe. To date, 5 trials are being managed and most of these trials are using the CLIN-NET and LAB-NET infrastructure of COMBACTE.

**VALUE-Dx ([www.value-dx.eu](http://www.value-dx.eu))**

VALUE-Dx (Value of diagnostics to combat antimicrobial resistance by optimizing antibiotic use) is the Innovative Medicines Initiative (IMI) project that brings together in vitro diagnostic companies and non-industry partners to combat antimicrobial resistance (AMR) and improve patient outcomes. To help build the medical and economic case for rapid diagnostics in the fight against antibiotic resistance, VALUE-Dx will establish a sustainable European Standardised Care Network which is adequately trained and resourced to conduct clinical trials. Currently, VALUE-Dx is conducting a point prevalence audit survey (PPAS) in 18 European countries to record information about patients who seek healthcare for community acquired acute respiratory tract infections (CA-ARTI), helping researchers to benchmark patterns of testing and antibiotic prescribing. Two clinical studies, to be conducted in the next winter seasons, are being designed to demonstrate the value of diagnostics in the optimal management of CA-ARTI in different European healthcare settings. UMCU leads the hospital-based study in VALUE-Dx, to be executed in about 10 European countries. It will enrol patients (including children) in Emergency Rooms presenting with CA-AI to determine the added values of Point-of-Care testing of respiratory pathogens on clinical decision making to withhold antibiotics and to hospitalize (or not) patients. The trial will start site selection in March 2020, with a focus on countries (and hospitals) where PoC testing has not yet been implemented, being countries in southern and eastern Europe.

**ECRAID-Plan ([www.ecraid.eu](http://www.ecraid.eu))**

Building on the foundations of the European consortia COMBACTE and PREPARE, ECRAID aims to advance clinical research in the field of infectious disease by further organizing and developing a European clinical research network. The network will function as the backbone of clinical research activities, providing an efficient infrastructure capable to perform all clinical trial aspects, from study design to scientific publication. All activities will be coordinated by a lean, centralized organization allowing easy access for all relevant stakeholders. The current ECRAID-Plan project
RECOVER Part B 4-5

is a two-year H2020 funded project (January 2019-Dec 2020) that will develop the business plan for ECRAID. ECRAID is aiming to launch its operations by the end of 2020.

Description of significant infrastructure, relevant to RECOVER

The existing network infrastructures of COMBACTE, PREPARE and VALUE-Dx allow the rapid clinical research response to the pandemic threat created by 2019-nCoV.
PARTNER 4: ERASMUS UNIVERSITY MEDICAL CENTER (ERASMUS MC)

Description of participant and main tasks

Erasmus MC is the largest university medical centre in the Netherlands. Erasmus University Medical Center Rotterdam is committed to a healthy population and excellence in healthcare through research and education (www.erasmusmc.nl). The center has broad expertise in various research fields, ranging from fundamental and clinical domains to public health and prevention, with an annual research budget of around €140 million. Erasmus MC holds over 90 projects funded by the European Commission, of which 85 Horizon 2020 projects including collaborations with partners from 56 countries worldwide. Bibliometric indicators place Erasmus MC in the top 20 of clinical medicine worldwide; its publications are cited 1.89 times the world average. In addition to scientific research, patient care and education are core tasks of Erasmus MC. It is the top referral centre for a region of about five million inhabitants. Erasmus MC is also the largest medical school in the Netherlands, with around 4,500 students and 220 PhD graduates in 2017, and offers BSc, MSc and PhD programs. Together, the students and around 16,500 employees at Erasmus MC improve the individual patient care and public health of tomorrow.

The Department of Viroscience at Erasmus MC (see www.virosciencelab.com) employs more than 110 persons of different disciplines and runs an extensive research program on viral infections of humans and animals, with specific interests in viral zoonoses, pathogenesis and transmission and natural and vaccine-induced immunity. There are 6 principal investigators at the professor level, each representing an essential skill in infectious diseases, including professors in 1) General Virology; 2) Molecular Virology; 3) Immunology; 4) Pathology; 5) Epidemiology; 6) Clinical Virology, as well as assistant/associate professors specialized in specific virus fields. Viruses under research include influenza A and B virus, RSV, hMPV, measles virus, coronaviruses, HIV-1, HIV-2, hepatitis A, B and C viruses, West Nile virus, Zika virus, Usutu virus, dengue viruses, Orthohantaviruses, lyssa viruses and herpes viruses. The department houses the National Influenza Centre, the national reference centre for emerging viral diseases, and the WHO collaborating centre for for arbovirus and viral haemorrhagic fevers reference and research. The department has built up an extensive track record in the identification of several novel human viruses, including human metapneumovirus (HMPV), human H5N1 infection in Hong Kong, SARS-CoV, hCoV-NL63 and MERS-CoV. In collaboration with the department of Zoology at Cambridge University, UK, the department has developed methods for improving human influenza virus surveillance and vaccine strain selection (2004), which have been adopted by the WHO as an integral part of the annual vaccine strain selection process. The department of Viroscience at EMC will deliver the co-Coordinator of RECOVER and will be involved in Wp5.

Profiles of main persons involved

Prof. Dr. Marion Koopmans (f): Department of Viroscience
Professor Marion Koopmans focuses her research on unravelling the modes of transmission of human and animal viruses, by developing genomic and serum profiling techniques for assessing exposure and infection to unravel these pathways, and to signal changes in transmission or disease impact. She focuses on global population level impact of rapidly spreading zoonotic virus infections, with special emphasis on foodborne transmission. As initiator of the global Noronet network (see www.noronet.nl), she has developed a global network of scientists sharing information on disease outbreaks into a jointly owned database to study norovirus diversity related to human health impact. Her aim is to provide insights that can be translated into concrete public health interventions. She coordinates a worldwide collaborative network of laboratories specialized in enteric viruses, funded through the European Commission DG Research (FP7) and DG Health and Consumers (SANCO), is the co-Coordinator of COMPARE and principal investigator/WP leader in EMERGE, PREPARE, and ZIKAlliance. Building from the norovirus work and molecular epidemiological expertise, she has expanded her research into emerging viral diseases that are recognized with increasing frequency. As Head of the Virology Reference Laboratory of the National Public Health Laboratory, a position she held from 2002 to 2014, she has been responsible for emerging disease preparedness, and coordination of the national laboratory response to such disease outbreaks, including SARS, pandemic influenza H1N1 2009, avian influenza and MERS. Building from those experiences, she developed an academic emerging disease preparedness research agenda at Erasmus MC as Head of the Department of Viroscience, combining basic laboratory science and tools with epidemiology to unravel causes, pathogenesis, sources and transmission routes of emerging viral diseases at the
Dr. Bart Haagmans (m): Department of Viroscience Dr. Bart Haagmans (male PhD) is a workgroup leader at the department of Viroscience of the Erasmus Medical Center in Rotterdam. His main field of interest is the pathogenesis of emerging viral infections including SARS and MERS coronavirus. He is a recognized leader in the field of coronaviruses and was involved in the characterization of the MERS-CoV genome and development of molecular and serological assays to detect MERS-CoV, but also different other emerging viruses. In addition, the viral receptor was identified and the dromedary camel was shown to act as the reservoir species. This led to testing a vaccine candidate that reduces the transmission of MERS-CoV by vaccinating dromedary camels, that will now be tested in a phase 1 trial in humans at Erasmus MC. These studies contributed to a more detailed understanding of the biology of this emerging virus and led to novel intervention strategies to contain the outbreak. In addition, genomes of several other novel viruses and their variants were characterised by by full genome analysis, including ZIKA virus and Ebola virus. Special emphasis was put also on developing protocols for diagnostic work with ebolavirus locally in western Africa. He is in charge of the existing biosafety laboratories currently operational at the Viroscience Department and is involved in building new animal biosafety level 3 laboratories, compulsory to perform research with highly pathogenic viruses, such as MERS and SARS coronavirus. Pipelines to generate nanobodies and single chain antibodies against MERS-CoV were established recently. He is also the author of more than 150 papers in peer-reviewed journals (h index of 51). Dr. Haagmans is co-coordinator of IMI-ZAPI, and Expert Consultant of WHO, FAO, OIE, Co-PI on CEPI-MERS on clinical evaluation of MVA-MERS-CoV candidate vaccine

Selection of relevant publications


List of relevant projects

PREPARE: www.prepare-europe.eu

The Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE) is a large scale European project, including 27 beneficiaries and is funded by the EU FP7 Programme. PREPARE aims for the creation of operational readiness for rapid deployment of harmonised European clinical studies for any infectious disease
outbreak and effective spread of evidence-based clinical guidelines via public health agencies to healthcare centres over the globe. To date, 5 trials are being managed and most of these trials are using the CLIN-NET and LAB-NET infrastructure of COMBACTE.

COMPARE: www.compare-europe.eu
The COllaborative Management Platform for detection and Analyses of (Re-) emerging and foodborne outbreaks in Europe (COMPARE) is an EU H2020 funded project, coordinated by DTU. COMPARE is a multidisciplinary research network that is set up with the common vision to become the enabling analytical framework and globally linked data and information sharing platform system for the rapid identification, containment and mitigation of emerging infectious diseases and foodborne outbreaks. The system sets out to integrate state-of-the-art strategies, tools, technologies and methods for collecting, processing and analysing sequence-based pathogen data in combination with associated (clinical, epidemiological and other) data, for the generation of actionable information to relevant authorities and other users in the human health, animal health and food safety domains.

VEO
VEO (Versatile Emerging infectious disease Observatory) is a research and innovation action funded by the European Commission’s Horizon2020 framework program, with 20 partners from 12 different countries, and a budget of 15 million euros. VEO will strive to establish an interactive virtual observatory for the generation and distribution of high-quality actionable information for evidence-based early warning, risk assessment and monitoring of emerging infectious diseases (EID) threats by public health actors and researchers in the One Health domain.

VEO partners’ ambition is to revolutionize the current ability to detect and analyze outbreaks of emerging disease at a much earlier stage than currently is possible, thus allowing time to respond rapidly to and seriously curtail their impact. Erasmus MC, represented by Prof. Marion Koopman, is the coordinator of the VEO project. The project started 1 January 2020, and will receive funding for 5 years. Emerging infectious diseases (EID) and antimicrobial resistance (AMR) are increasing due to global changes that have a fundamental impact on the dynamics of infectious diseases, challenging the existing global health infrastructure and organization. The lessons from recent outbreaks show that detection of outbreaks often is delayed. Rapid identification is essential to reduce the impact and costs of outbreaks, but it is a challenge to be prepared globally as preparedness competes with other priorities in healthcare and public health. As a major part of EID and AMR come from animals, a true shift in ability to detect would come from deep understanding the factors that drive their emergence, focusing on the complex interplay of environmental and human factors that drive disease dynamics. The VEO consortium is highly complementary in terms of European geographic coverage, expertise and disciplinary backgrounds and roles in EID preparedness and response.

ECRAID-Plan (www.ecraid.eu)
Building on the foundations of the European consortia COMBACTE and PREPARE, ECRAID aims to advance clinical research in the field of infectious disease by further organizing and developing a European clinical research network. The network will function as the backbone of clinical research activities, providing an efficient infrastructure capable to perform all clinical trial aspects, from study design to scientific publication. All activities will be coordinated by a lean, centralized organization allowing easy access for all relevant stakeholders. The current ECRAID-Plan project is a two-year H2020 funded project (January 2019-Dec 2020) that will develop the business plan for ECRAID. ECRAID is aiming to launch its operations by the end of 2020.

EVD-LabNet: https://www.evd-labnet.eu/
EVD-LabNet is a European Expert Laboratory Network for detection and surveillance of (re)emerging viral diseases in Europe funded by the ECDC. A prerequisite for identification, surveillance, assessment and communication of current and emerging infectious disease threats to Public Health, is the availability of a reliable capability and sufficient capacity of diagnostic and reference laboratory service. To facilitate this, ECDC has contracted Erasmus MC to establish and operate an expert laboratory network that provides laboratory and expertise support to the ECDC and member European laboratories that are involved in diagnostics of (re)emerging viral diseases. To this effect the expert network supports individual patient care, surveillance and outbreak response by provision to ECDC, other European networks and member laboratories of information on target viruses, access to (reference) diagnostics and a state-of-the-art European diagnostic portfolio and diagnostic capacity and capability.
Furthermore EVD-LabNet provides training workshops based on needs within the network, establishes Twinning partnerships and organises yearly meetings to strengthen the coherence of the network and to provide a platform for knowledge exchange. The network covers all European countries (not only EU/EEA) to properly reflect and respond to the transboundary aspects of emerging infectious diseases; 72 expert laboratories in 38 countries. It also aims to actively connect to other European emerging infectious disease preparedness and response networks.

ZikAlliance: https://zikalliance.tghn.org/
ZikAlliance is a multinational and multi-disciplinary research consortium comprised of 53 partners worldwide, funded by the European Union's Horizon 2020 Research and Innovation Programme. The project will investigate clinical, fundamental, environmental and social aspects of ZIKV infection. In particular, ZikAlliance will focus on the impact of ZIKV infection during pregnancy and the natural history of ZIKV in humans and their environment. ZikAlliance works closely with two other European Union-funded consortia, ZIKAction and ZikaPLAN, to establish a Latin American and Caribbean network. This network will address the broader issue of building local capacity in Latin America to prepare for and rapidly launch a large-scale research response to emerging infectious disease threats. The three consortia also have common bodies for the global management of scientific programs, communication, and ethical, regulatory and legal issues.

EVAg: https://www.european-virus-archive.com/
The European Virus Archive (EVAg) is a non-for-profit international organization that mobilises a global network including 26 EU and non-EU partners and 14 associate institutions with expertise in virology to collect, amplify, characterize, standardize, authenticate, distribute, track and collect viruses and derived products. Most of the partners hold BSL3 facilities and 14 of them have BSL4 capacities. EVAg is dedicated to the characterization, conservation, production, distribution and characterisation of biological materials in the field of virology. EVAg aims at distributing gold standard quality virus and virus derived material to the scientific community. It acts under the WHO umbrella to supply diagnostic reagents to countries facing emerging viral diseases epidemics. For that purpose, EVAg maintains high control standards and develops appropriate methods directly relevant to human and animal virology.

ZAPI: http://www.zapi-imi.eu/about-zapi
The new Zoonoses Anticipation and Preparedness Initiative (ZAPI), part of the Innovative Medicines Initiative (IMI) public-private partnership, aims to enable swift response to major new infectious disease threats in Europe and throughout the world by designing new manufacturing processes (up to large scale) for delivering effective control tools (vaccines, antibodies/antibody-like molecules) against (re-)emerging zoonotic diseases with pandemic potential within a few months after the occurrence of first cases.

ZAPI is a 5 years collaborative partnership between more than 20 European partners, including leading human and veterinary research institutions, non-governmental organizations, regulatory agencies, expert academic groups, and vaccine and biotech manufacturers. With more than 22 million euros in funding, ZAPI is the first true "One Health" project within the scope of IMI and unites experts in animal health and human health.
**PARTNER 5: UNIVERSITY OF OXFORD (UOXF)**

The University of Oxford ranks in the top three Universities for research in the UK and the top five in the world. The Centre for Tropical Medicine, which is part of the Nuffield Department of Medicine, is based within the Medical Sciences Division of the University of Oxford. The Nuffield Department of Medicine (NDM) employs approximately 1000 research staff working in a range of basic science and clinical disciplines and involved in world-class clinical trials and translational research. The Nuffield Department of Medicine in Oxford hosts a number of research groups complimentary to and directly involved in PREPARE and ZIKAlliance, including the International Severe Acute Respiratory Consortium (ISARIC – Peter Horby). There are very strong links within the University with the Clinical Trials Service Unit (Richard Peto), the Centre for Human Genetics (Peter Donnelly), the ETHOX Centre (Michael Parker) and the Department of Public Health (Rory Collins). Strong linkages with the overseas programmes and Oxford research groups within Medical Sciences and the wider University give the Oxford Centre groups unique access to collaborations and networks covering respiratory research globally. The Centre provides resources and other support to enable research to be conducted in the most efficient and effective way whilst enabling the training of the next generation of world-class scientists and clinicians.

The Nuffield Department of Primary Care Health Sciences was ranked the top centre for primary care research in the UK in the 2014 national Research Excellence Framework exercise. We were similarly judged a top centre on our 1996–2008 assessments, so have been one of the world’s most important primary care centres for almost 20 years. Chris Butler is Director of the University of Oxford Primary Care Clinical Trials Unit, which has over 80 members of staff and a portfolio of 43 projects with a total value of £34m. He leads WP4 in PREPARE, which included the ALIC4E trial on ILI in primary care, which was published in 2020 in the lancet and is already impacting on care for ILI worldwide. The Department hosts the National Institute of Health Research Institute Diagnostics Evidence Cooperative to identify new and emerging IVDs relevant to primary care settings, to ultimately improve the efficiency of care of patients by improving access, accuracy and patient satisfaction with IVDs in primary care. Chris Butler is the Director, and experienced clinical trialist, General Practitioner, and infections researcher, Gail Hayward, is the Deputy Director. It also hosts the Centre for Evidence based Medicine. Chris Butler leads the Common Infections Research Group, that includes trialists and a strong social science team led by Sarah Tonkin-Crine that conducts process evaluations embedded within trials, and achieves a rigours undeedening of relevant perceptions co clinicians, patients and the public into infections and pandemic management, that feel in to behavioural interventions and evidence based risk communication strategy development. The Department provides undergraduate education in primary care medicine and a thriving Master’s program in Evidence based Health care and a sought-after Doctoral program.

Profiles of main persons involved

**Prof. dr. Peter Horby (m):** Peter Horby is Professor of Emerging Infectious Diseases and Global Health at the University of Oxford, UK. He has led research on a range of emerging and epidemic infections, including variant CJD, SARS, avian influenza A/H5N1 and A/H7N9, dengue, cholera, measles, Streptococcus suis, severe EV71, and Ebola. He is a member of the UK Department of Health New and Emerging Respiratory Virus Threats Advisory Group and the UK Public Health Rapid Support Team, a specialist team of health experts ready to be deployed to tackle outbreaks of deadly disease anywhere in the world within 48 hours. Peter is an advisor to the World Health Organization on the research agenda for influenza; the prioritization of severe emerging infectious diseases for research and development; and clinical trial designs for epidemic-prone infections. Peter Horby leads PREPARE WP2 "PRIME: Clinical protocols and guidelines for ID management in Europe" and WP3 "Multi-centre EuRopean study of MAjor Infectious Disease Syndromes (MERMAIDS)". He is the Coordinator of ALERRT and Chair of the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC).

**Prof. dr. Chris Butler (m):** Chris Butler, (>370 publications; h-index = 64) is a National Institute of Health Research Senior Investigator and Fellow of the Academy of Medical Sciences, and is professor of primary care at the University of Oxford’s Nuffield Department of Primary Care Health Sciences and professorial fellow at Trinity College. He is the Clinical Director of the University of Oxford Primary Care Clinical Trials Unit, and of the NIHR
Dr. Nina Gobat (f): Nina Gobat, PhD is a post-doctoral senior researcher with a background in health, behavioural and social sciences. Her research focus is on operational aspects of epidemic-relevant research. Much of this work was conducted under WP1 of PREPARE, which focused on identifying solutions to ethical, administrative, regulatory and logistical barriers to epidemic-relevant clinical studies in Europe. As part of this role, Nina established the PREPARE community advisory board. In addition, Nina was closely involved in developing and mobilising PREPARE’s outbreak response protocols. Prior to this, Nina’s research focused on the design and evaluation of complex interventions in public health and healthcare settings. Nina has expertise in both qualitative and quantitative research methods and in facilitating patient and public involvement in research. Additionally, Nina has over 15 years of clinical, teaching and supervisory experience and has worked in health service development and management roles. Nina is the social science focal point for the research group in the Global Outbreak Alert and Response Network (GOARN).

Dr. Sarah Tonkin Crine (f): Sarah Tonkin-Crine, PhD CPsychol is a registered Health Psychologist and senior researcher. Her research focusses on developing and evaluating behavioural interventions to improve healthcare delivery and patient health outcomes. She has expertise in using behavioural science and mixed methods approaches alongside clinical trials related to tackling antibiotic resistance. She has previously led a number of international qualitative studies looking at health service delivery and clinician behaviour change across multiple European countries. She is responsible for leading behavior research projects within the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Healthcare Associated Infections and Antibiotic Resistance at the University of Oxford in partnership with Public Health England. She is also an expert advisor on behavior for the UK Department of Health’s Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infections (APRHAI).

Dr Gail Hayward (f): Gail Hayward MRCGP D.Phil is an Associate Professor of Primary Care at the University of Oxford and a salaried GP. She is the Deputy Director of the National Institute for Health Research MedTech and IVD Cooperative, which aims to develop and evaluate diagnostic technology which is fit for purpose in community settings. Her research focusses on the diagnosis and management of common infections in primary care. She is chief investigator of MERIT, a randomized trial evaluating the benefit of D-Mannose in prophylaxis of recurrent UTI, and principle or co-investigator on a number of collaborative grants working with industry to evaluate their diagnostics in community settings. She also leads on qualitative studies exploring barriers and facilitators to novel diagnostics and patient and clinician experience of serious infections. She is a member of UK Antimicrobial Resistance Diagnostics Programme Board and the British Society for Antimicrobial Chemotherapy Board.

Selection of relevant publications

RECOVER


List of relevant projects

**PREPARE**: [www.prepare-europe.eu](http://www.prepare-europe.eu)

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**ALERRT**: [https://www.alerrt.global/](https://www.alerrt.global/)

ALERRT (African coALition for Epidemic Research, Response and Training) combines the strengths of leading African and European partners in (Re-)emerging and Epidemic-Prone Infectious Diseases (REPID) clinical research, preparedness and response. It builds on efforts by the EDCTP Networks of Excellence WANETAM, CANTAM and EACCR, and internationally well-embedded research and training partners with extensive operational experience in outbreak preparedness and response, and the associated challenges in sub-Saharan Africa (SSA). The purpose of ALERRT is to reduce the public health and socio-economic impact of REPID in SSA. This will be achieved by building a sustainable clinical and laboratory research preparedness and response network, with the operational readiness to rapidly implement clinical and laboratory research in support of REPID control efforts at local, regional
International Severe Acute Respiratory and emerging Infections Consortium (ISARIC)

ISARIC is a global federation of over 50 clinical research networks. ISARIC’s mission is both to conduct clinical research in the inter-epidemic period and during outbreaks. ISARIC works in very close partnership with the WHO Emerging Diseases Clinical Assessment and Research Network (EDCARN) and has made significant contributions to building capacity, linking researchers, developing generic clinical trial protocols, identifying ethical and legal barriers, and responding to outbreaks. Horby has been a member of ISARIC since its inception in 2012 and became the Chair in 2016. In this role Horby is a member of the WHO expert working groups on clinical trial design for outbreaks, and on pathogen prioritization for research and development.

VALUE-Dx: https://value-dx.eu/

VALUE-Dx (Value of diagnostics to combat antimicrobial resistance by optimizing antibiotic use) is the Innovative Medicines Initiative (IMI) project that brings together in vitro diagnostic companies and non-industry partners to combat antimicrobial resistance (AMR) and improve patient outcomes. To help build the medical and economic case for rapid diagnostics in the fight against antibiotic resistance, VALUE-Dx will establish a sustainable European Standardised Care Network which is adequately trained and resourced to conduct clinical trials. Currently, VALUE-Dx is conducting a point prevalence audit survey (PPAS) in 18 European countries to record information about patients who seek healthcare for community acquired acute respiratory tract infections (CA-ARTI), helping researchers to benchmark patterns of testing and antibiotic prescribing. Two clinical studies, to be conducted in the next winter seasons, are being designed to demonstrate the value of diagnostics in the optimal management of CA-ARTI in different European healthcare settings.

ECRAID-Plan (www.ecraid.eu)

Building on the foundations of the European consortia COMBACTE and PREPARE, ECRAID aims to advance clinical research in the field of infectious disease by further organizing and developing a European clinical research network. The network will function as the backbone of clinical research activities, providing an efficient infrastructure capable to perform all clinical trial aspects, from study design to scientific publication. All activities will be coordinated by a lean, centralized organization allowing easy access for all relevant stakeholders. The current ECRAID-Plan project is a two-year H2020 funded project (January 2019-Dec 2020) that will develop the business plan for ECRAID. ECRAID is aiming to launch its operations by the end of 2020.

Description of significant infrastructure, relevant to RECOVER

The Clinical Trials Unit supports investigator led multi-centre collaborative studies involving researchers from the Department of Primary Care Health Sciences and beyond. This is the largest primary care clinical trials unit in the UK with 80 staff and 59 studies; geographical reach from Wales to East of England and from the South Coast to Scotland. Oxford hosts the National Institute for health Research (NIHR) Community Healthcare Medical Devices and In Vitry Diagnostics supports industry to improve the implementation and uptake of in vitro diagnostics in primary care working with over 100 companies, winning collaborative grants (>£17m).
PARTNER 6: CHARITÉ UNIVERSITÄTSME dizin BERLIN (CHARITÉ)

Description of participant and main tasks

Charité is one of the largest university medical centres in Europe. All of our clinical care, research and teaching is delivered by physicians and researchers of the highest international standard. Charité proudly lays claim to more than half of all German Nobel Prize winners in Physiology or Medicine, including Emil von Behring, Robert Koch, and Paul Ehrlich. Charité is internationally renowned for its excellence in teaching and training. Charité – Universitätsmedizin Berlin represents a single medical faculty, which serves both Humboldt Universität zu Berlin and Freie Universität Berlin. Charité extends over four campuses, and has close to 100 different Departments and Institutes, which make up a total of 17 different CharitéCenters. Having marked its 300-year anniversary in 2010, Charité is now one of the largest employers in Berlin, employing 14,576 staff (or 18,010 if including its subsidiaries), and with a total annual turnover of €1.8 billion.

Profiles of main persons involved

Prof. dr. Christian Drosten (m): Christian Drosten started in 2000 in Bernhard Nocht Institute for Tropical Medicine, Hamburg and received a full approval as Physician in 2002. He became a Board-Certified Physician for Virology, Microbiology and Infection Epidemiology in 2006. His last position title in the institute was Head of Unit of Clinical Virology.

In 2007, he moved to the University of Bonn where he was appointed as a full Professor of Medicine. In this institute he served as the head of Institute of Virology. Christian published often in prestigious international scientific journals during this period. Since 2017, Christian moved to the Charité - Universitätsmedizin Berlin where he serves as a full Professor of Medicine, and became the head of the Institute of Virology. His major research interests (among others) are medical virology, viral evolution and ecology, epidemic preparedness research, coronaviruses.

Charité – Universitätsmedizin Berlin has a global network of partners. The health care-related challenges facing us today require intensive efforts to establish both national and international collaborations involving both treatment centres and research and teaching establishments. Cross-border cooperation with top-level partners will ensure Charité maintains its leading position as one of Europe’s largest university hospitals.

Selection of relevant publications

List of relevant projects

**PREPARE:** [www.prepare-europe.eu](http://www.prepare-europe.eu)
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The COllaborative Management Platform for detection and Analyses of (Re-) emerging and foodborne outbreaks in Europe (COMPARE) is an EU H2020 funded project, coordinated by DTU. COMPARE is a multidisciplinary research network that is set up with the common vision to become the enabling analytical framework and globally linked data and information sharing platform system for the rapid identification, containment and mitigation of emerging infectious diseases and foodborne outbreaks. The system sets out to integrate state-of-the-art strategies, tools, technologies and methods for collecting, processing and analysing sequence-based pathogen data in combination with associated (clinical, epidemiological and other) data, for the generation of actionable information to relevant authorities and other users in the human health, animal health and food safety domains.

**EVAg:** [https://www.european-virus-archive.com/](https://www.european-virus-archive.com/)
The European Virus Archive (EVAg) is a non-for-profit international organization that mobilises a global network including 26 EU and non-EU partners and 14 associate institutions with expertise in virology to collect, amplify, characterize, standardize, authenticate, distribute, track and collect viruses and derived products. Most of the partners hold BSL3 facilities and 14 of them have BSL4 capacities. EVAg is dedicated to the characterization, conservation, production, distribution and characterisation of biological materials in the field of virology. EVAg aims at distributing gold standard quality virus and virus derived material to the scientific community. It acts under the WHO umbrella to supply diagnostic reagents to countries facing emerging viral diseases epidemics. For that purpose, EVAg maintains high control standards and develops appropriate methods directly relevant to human and animal virology.

Description of significant infrastructure, relevant to RECOVER

All lab facilities on board for work with 2019-nCoV: Amongst others BSL-4 laboratories. Permission to work with 2019-nCoV and SARS-CoV.

The lab is appointed by the German Ministry of Health as the national reference lab (“Konsiliarlabor”) for coronaviruses. In this function, we perform reference diagnostics and provide methodologies to laboratories across the country. We receive samples from clinical cases of human coronavirus, MERS-coronavirus, and nCoV-infection on a regular basis. We currently have clinical materials from the whole clinical course of ca. 12 patients available. A large biobank of respiratory samples is also available and constantly updated.

The institute overall coordinates research consortia across the thematic field of emerging infections. For instance, DFG focus program 1596 deals with ecology and species barriers of emerging viral diseases. The RAPID consortium funded by the German ministry of research and education tries to develop novel approaches to risk assessments in relation to emerging respiratory viruses, exemplified by the MERS agent. RAPID is part of the National Research Network on Zoonotic Infections. Within the German Center for Infection Research, we conceptualize a work program on emerging viruses detection and preparedness. We are members of the European Union consortia COMPARE, dealing with sequencing-based virus surveillance, as well as PREPARE dealing with clinical preparedness against pandemic infections. We are a founding member of the European Virus Archive (EVAg), an EU infrastructure facilitating the provision of reference virus material for research and development purposes.
PARTNER 7: INSTITUT NATIONAL DE LA SANTÉ ET DE LA RECHERCHE MÉDICALE (INSERM)

Description of participant and main tasks

https://www.inserm.fr/en

Founded in 1964, Inserm (Institut National de la santé et de la recherche médicale) is a public scientific and technological institute which operates under the joint authority of the French Ministries of Health and Research. The institute is dedicated to biomedical research and human health, and is involved in the entire range of activities from the laboratory to the patient’s bedside. It also partners with the most prestigious research institutions in the world that are committed to scientific challenges and progress in these fields. Since its foundation, Inserm has played a part in many key medical advances, including the first prenatal diagnostic tests, understanding of the HLA system, the first in vitro fertilization, identification of the AIDS virus, radiotherapy for cancer, the first skin graft, deep brain stimulation, and gene therapy. Inserm is the leading European academic biomedical research institution, and with nearly 12,000 publications a year, is second in the world only to the National Institutes of Health (NIH). According to the 2016 ranking by Thomson-Reuters, Inserm is also the world’s 9th most innovative public research organization.

Profiles of main persons involved

Prof. dr. Xavier Duval (m): Xavier Duval is infectious diseases specialist, professor of therapeutics, doctor of science, director of the medical-administrative department PRISME (Pharmacy, health products, clinical research, medical information, hospital public health, evaluation methods, epidemiology) of the APHP-North University of Paris, coordinator of the Clinical Investigation Centre Inserm 1425 of the Groupe Hospitalier Paris Nord-Val de Seine (HUPNVS), member of the IAME Inserm Unit 1137 (Infection-Antimicrobial Modelling-Evolution) in the BIPID team (Biostatistical Modelling, Pharmacometrics and Clinical Investigation in Infectious Diseases) of Pr France Mentré. He coordinates research projects in several fields of infectiology, in particular on respiratory infectious diseases including influenza and emerging diseases. He has led or co-led more than 20 clinical trials or cohort studies including patients or healthy volunteers and is author or co-author of more than 290 publications, which are referenced in Pubmed.

Dr. Vittoria Colizza. (f): Vittoria Colizza completed her undergraduate studies in Physics at the University of Rome Sapienza, Italy, in 2001 and received her PhD in Statistical and Biological Physics at the International School for Advanced Studies in Trieste, Italy, in 2004. She then spent 3 years at the Indiana University School of Informatics in Bloomington, IN, USA, first as a post-doc and then as a Visiting Assistant Professor. In 2007 she joined the ISI Foundation in Turin, Italy, where she started a new lab after being awarded a Starting Independent Career Grant in Life Sciences by the European Research Council Ideas Program (more info on the EpiFor project webpage). In 2011 Vittoria joined the INSERM (French National Institute for Health and Medical Research) in Paris where she now leads the EPIcx lab within the Equipe surveillance and modeling of communicable diseases of the Pierre Louis Institute of Epidemiology and Public Health (IPLESP). She works on the characterization and modeling of the spread of emerging infectious diseases, by integrating methods of complex systems with statistical physics approaches, computational sciences, geographic information systems, and mathematical epidemiology. In 2017 she was promoted Research Director at INSERM.

Colizza’s work is centered in the development of data-driven mathematical and computational models to solve problems of infectious disease dynamics and public health. Using large-scale data characterizing contacts, behaviors, and mobility of hosts from a variety of sources and sensors (face-to-face interactions, contact matrices, commuting, air travel, migrations, trade movements, call detail records from mobile phones, etc.), her research explores how disease diffusion in space is shaped by hosts’ behavior. Applications range from human epidemics (e.g. 2009 H1N1 pandemic influenza, MERS-CoV epidemic, Ebola virus disease epidemic, seasonal flu, AMR pathogens) to animal epidemics (e.g. bovine brucellosis and tuberculosis, bovine viral diarrhea, rabies in dogs and
Dr. Jérémie Guedj (m) Jérémie Guedj’s is an engineer by training and received his PhD in biostatistics from University Bordeaux 2 in 2006. He then did postdocs in Israel and in the US where he specialized on the modelling of host/pathogen interaction, in particular in HIV and viral hepatitis. In 2011 he was recruited as a researcher at INSERM and oriented his research towards the pharmacometrics of infectious diseases, i.e., the development of mathematical and statistical models to optimize the response to antiviral treatment. He has developed expertise in many fields, including chronic viral infections, antibiotic resistance, haemorrhagic fever viruses.

Prof. dr. France Mentré (f): France Mentré is Professor of Biostatistics in the School of Medicine of University of Paris. She leads an INSERM research team on Biostatistical Modelling and Pharmacometrics in treatment of Infectious Diseases. She has worked on development and application of methods for nonlinear mixed-effects models and pharmacometrics for more than 30 years. She applies these models to understand the variability in the response to anti-infective agents. She has published more than 250 articles in biostatistics, pharmacometrics, clinical pharmacology or medical research. She is editor in chief since October 2018 of CPT: Pharmacometrics and System Pharmacology. She was actively involved in the H2020 grant ‘Reaction’ on evaluation of favipiravir in Ebola virus disease, mainly in pharmacokinetic and viral dynamic modelling in patients and animals.

Selection of relevant publications


List of relevant projects

REACTing https://reacting.inserm.fr/

REACTing is a multi-disciplinary collaborative network of French research institutions working on emerging infectious diseases, which aims to prepare and respond to epidemics. REACTing aims to forge a new dynamic to face health emergency situations by contributing to national health decisions and to international efforts to control emerging infectious threats. It covers a wide array of research fields in human and animal health: surveillance, public health, clinical research, mathematical modelling, diagnosis and pathogen characterization, social sciences and ethical and regulatory capacities. It brings together excellent research groups, institutions and laboratories in order to prepare and deal with unforeseeable emerging infectious threats. The role of REACTing in the 2019-nCoV outbreak is to coordinate French research response. Since the beginning of the 2019-nCoV outbreak, REACTing is playing a key role in the coordination and information sharing regarding 2019-nCoV outbreak in France.

GrippeNet.fr

GrippeNet.fr is a participatory surveillance system collecting voluntary reports of influenza-related symptoms through a dedicated website (https://www.grippenet.fr) where individuals also provide profile information. Data are collected on a weekly basis through a symptom survey. The system was launched during the 2011-2012 seasonal flu epidemic as a collaboration between Inserm, Sorbonne Universite and Sante publique France. It currently counts approximately 6,000 volunteering participants. The system has also been used for studying the perception,
awareness and sentiment towards vaccination, and also to characterize health-seeking behaviour. In RECOVER, GrippeNet.fr will be used to measure awareness/perceived risks/trust/attitudes of participants towards the 2019-nCoV epidemic. In case an epidemic develops in France, GrippeNet.fr will be used for monitoring changes of behaviour during the different phases of the epidemic (e.g. health-seeking behaviour, isolation, social distancing, telework, etc.). This same study will be run also in 6 other countries in Europe (Italy, Denmark, Spain, Switzerland, Portugal), partners of GrippeNet.fr under the Influenzanet network.

**H2020 project MOOD**

MOnitoring Outbreak events for Disease surveillance in a data science context (MOOD) is a EU project (H2020-874850) aimed at harnessing the data mining and analytical techniques to the big data originating from multiple sources to improve detection, monitoring, and assessment of emerging diseases in Europe. To this end, MOOD will establish a framework and visualisation platform allowing real-time analysis and interpretation of epidemiological and genetic data in combination with environmental and socio-economic covariates in an integrated inter-sectoral, interdisciplinary, One health approach: 1) Data mining methods for collecting and combining heterogeneous Big data, 2) A network of disease experts to define drivers of disease emergence, 3) Data analysis methods applied to the Big data to model disease emergence and spread, 4) Ready-to-use online platform destined to end users, i.e. national and international human and veterinary public health organizations, tailored to their needs, complimented with capacity building and network of disease experts to facilitate risk assessment of detected signals. INSERM (Vittoria Colizza) is leader of WP on Modeling.

**Description of significant infrastructure, relevant to RECOVER**

GrippeNet.fr (see above)
PARTNER 8: ACADEMIC MEDICAL CENTER (AMC)

Description of participant and main tasks

The Academic Medical Center (AMC) houses the university hospital and the medical faculty of the University of Amsterdam and is one of the largest hospitals in the Netherlands with 1002 beds, 60,000 admissions and 350,000 outpatient visits each year. Infectious Diseases represents a priority topic of clinical, applied and basic research at the AMC, integrated in a multidisciplinary fashion at the Center for Infection and Immunity AMC (CINIMA). The Department of Medical Microbiology employs around 180 people and is responsible for infectious disease diagnostics and clinical consultations, for microbiology education and training for (bio)medical students and residents in clinical microbiology, and for basic, translational and clinical research in bacteriology, virology and parasitology. It houses the Dutch national reference laboratories for bacterial meningitis and for leptospirosis, as well as state- of-the art culture, serological and molecular laboratory facilities up to biosafety level 3. The Department of Microbiology (Menno de Jong) is the co-coordinator of PREPARE and leads WP6 PATHOS (patient-oriented pathogenesis studies) in PREPARE and is a partner in COMPARE.

Profiles of main persons involved

Prof. dr. Menno de Jong (m): Menno de Jong is clinical microbiologist, professor of clinical virology and head of the Department of Medical Microbiology. Inspired by his previous work in southeast Asia, where he set up and headed the virology department at the Oxford University Clinical Research Unit in Vietnam, his current research remains focused on understanding the emergence and pathogenesis of emerging infectious disease and improving clinical and diagnostic management, by observational and interventional clinical studies in an international context, supported by experimental research. He was involved in the launch and further development of international initiatives geared towards timely and harmonised clinical research in the face of epidemics, such as the Southeast Asia Infectious and EmergingInfectious Disease Clinical Research Network (SEAICRN) and the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC). He sits on the ISARIC Executive Board and is scientific co-chair of the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) secretariat.

Selection of relevant publications


List of relevant projects

PREPARE: www.prepare-europe.eu

The Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE) is a large scale European project, including 27 beneficiaries and is funded by the EU FP7 Programme. PREPARE aims for the creation of operational readiness for rapid deployment of harmonised European clinical studies for any infectious disease outbreak and effective spread of evidence-based clinical guidelines via public health agencies to healthcare centres.
over the globe. To date, 5 trials are being managed and most of these trials are using the CLIN-NET and LAB-NET infrastructure of COMBACTE.

**COMPARE: www.compare-europe.eu**

The COllaborative Management Platform for detection and Analyses of (Re-) emerging and foodborne outbreaks in Europe (COMPARE) is an EU H2020 funded project, coordinated by DTU. COMPARE is a multidisciplinary research network that is set up with the common vision to become the enabling analytical framework and globally linked data and information sharing platform system for the rapid identification, containment and mitigation of emerging infectious diseases and foodborne outbreaks. The system sets out to integrate state-of-the-art strategies, tools, technologies and methods for collecting, processing and analysing sequence-based pathogen data in combination with associated (clinical, epidemiological and other) data, for the generation of actionable information to relevant authorities and other users in the human health, animal health and food safety domains.

**ECRAID-Plan (www.ecraid.eu)**

Building on the foundations of the European consortia COMBACTE and PREPARE, ECRAID aims to advance clinical research in the field of infectious disease by further organizing and developing a European clinical research network. The network will function as the backbone of clinical research activities, providing an efficient infrastructure capable to perform all clinical trial aspects, from study design to scientific publication. All activities will be coordinated by a lean, centralized organization allowing easy access for all relevant stakeholders. The current ECRAID-Plan project is a two-year H2020 funded project (January 2019-Dec 2020) that will develop the business plan for ECRAID. ECRAID is aiming to launch its operations by the end of 2020.

**GloPID-R-Sec: [https://www.glopid-r.org/](https://www.glopid-r.org/)**

GloPID-R-Sec is the EU-funded secretariat (2015-2020) which supports activities of the Global Research Collaboration for Infectious Disease Preparedness (GloPID; [www.glopid-r.org](http://www.glopid-r.org)), a global network of research funding organizations focused on facilitating timely and effective research responses to new or re-emerging infectious disease outbreaks of pandemic potential. De Jong is scientific co-chair of the secretariat.

**SEAICRN: [www.seaicrn.org](http://www.seaicrn.org)**

The Southeast Asia Infectious Disease Clinical Research Network was launched in 2005 with funding from the US NIAID and the UK Wellcome Trust in response to the emergence of H5N1 avian influenza and other emerging infectious diseases in the region. SEAICRN is a network of hospitals and research institutions in Vietnam, Thailand and Indonesia, aimed at conducting collaborative clinical research that addresses emerging threats and improve the clinical management of infectious diseases of public health importance. As chair of the SEAICRN Laboratory Committee, De Jong was responsible for coordinating the development of diagnostic capacity in participating hospitals to support clinical studies, including the first ever randomized controlled trial addressing treatment of influenza in hospitalized patients.

**Description of significant infrastructure, relevant to RECOVER**

The Department of Medical Microbiology houses (tissue) culture, serological and molecular laboratory facilities up to biosafety level 3 and has unlimited access to the Amsterdam UMC central genomics facility, housing a range of state-of-the-art sequencing platforms. In the context of the PREPARE project analysis pipelines have been developed and are available for high throughput gene expression profiling studies. Computational and bioinformatic expertise is concentrated in the Departments Laboratory of Applied Evolutionary Biology. Extensive computational capacity is available through hospital and university (LISA) computer clusters.
**PARTNER 9: FONDAZIONE PENTA (PENTA)**

**Description of participant and main tasks**

The Paediatric European Network for Treatment of AIDS (PENTA, www.penta-id.org) was established in 1991 by collaborating paediatric HIV centres across Europe to construct a large cohort of children infected with HIV and undertake independent clinical trials addressing questions about antiretroviral therapy (ART) in HIV infected children where answers could not be extrapolated from trials in adults. The PENTA Foundation was set up in 2004 as the legal body coordinating the PENTA network, and seeks to discover and implement the best ways to prevent, diagnose and treat diseases in children.

In 2011 PENTA officially became PENTA-ID (Infectious Diseases), an evolution stemming from the need to integrate the expertise acquired by PENTA in more than 20 years of successful activity in the area of HIV and the need for research in other paediatric infectious diseases. Today the network benefits from international recognition, wide geographical representativeness with over 90 centers in 18 countries, very high-quality research, an outstanding track record and diversified public and private funding. PENTA-ID has been recognized as a Level-1 Network for paediatric infectious disease in Europe by EnprEMA. Current activities range from coordinating clinical trials and epidemiologic studies to research infrastructure and capacity building activities, development of treatment guidelines and training/educational programmes in both HIV and non-HIV areas. Through this research and partnership, PENTA is a leading organization dedicated to the health of children, with the aim to reduce the frequency and consequences of childhood infection.

The PENTA Foundation is the coordinator of the IMI2-funded CoLLaborative Network for European Clinical Trials For Children (c4c), a large collaborative effort aiming to overcome the barriers in paediatric medicines development by building, implementing and testing a robust, sustainable and integrated European platform for paediatric trial delivery. PENTA also coordinates 4 large EU funded projects (NeoVanc, ZIKAction, REACH, PEDICAP) and is involved as a key Partner in other 7 large EU-funded research Networks (EPTRI, EMPIRCAL, BREATHER+, VALUE-DX, ECRAID, RESCEU, COMBACTE). PENTA also coordinates the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC). As a Partner within the Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE) Consortium, PENTA coordinates the paediatric activities. PENTA is also coordinator of the Industry-sponsored EPIICAL project, an innovative global platform for development and testing of immunotherapeutic strategies among HIV infected children and is key Partner in the newly developed antibiotic resistance initiative promoted by DNDi-GARDP.

**Profiles of main persons involved**

**Prof. dr. Carlo Giaquinto(m):** Carlo Giaquinto full professor of Paediatrics at the University of Padova and Head of the Paediatric AIDS Centre. President of Fondazione Penta (www.pentafoundation.org). He has been coordinating 15 large EU funded projects (including EDCTP and IMI) from 1992, including, PENTA/LABNET, NEOMERO, NeoVanc, GRIP, ZIKAction, c4c, REACH, EPIICAL etc. Recipient of the Bill Marshall award in 2017, he is author of more than 30 papers in international peer-reviewed journals.

**Dr. Julia Bielicki (f):** Julia Bielicki obtained her medical degree from the University of Cambridge (2004) and a Master of Public Health from the London School of Hygiene and tropical Medicine (2011). Dr Bielicki completed her clinical training in Paediatrics (2009) and Infectious Diseases (2017) in the UK and Switzerland. Since 2015, Dr Bielicki has held a joint appointment as the lead for infection prevention and control and consultant in paediatric infectious diseases at the University of Basel Children’s Hospital and as a Senior Lecturer in paediatric infectious diseases at St George’s University of London. In Basel, Dr. Bielicki coordinates the paediatric study centre, an infrastructure supporting clinical research currently involved in 17 studies across different paediatric disciplines. She has been involved in the coordinating or leadership teams of several national and international research projects, several of which focus on the optimal management of childhood acute respiratory tract infection, including ARPEC, PREPARE, CAP-IT (NIHR-funded), KIDS-STEP (SNSF-funded) and PediCAP.
Selection of relevant publications


List of relevant projects

PREPARE: www.prepare-europe.eu
The Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE) is a large scale European project, including 27 beneficiaries and is funded by the EU FP7 Programme. PREPARE aims for the creation of operational readiness for rapid deployment of harmonised European clinical studies for any infectious disease outbreak and effective spread of evidence-based clinical guidelines via public health agencies to healthcare centres over the globe. To date, 5 trials are being managed and most of these trials are using the CLIN-NET and LAB-NET infrastructure of COMBACTE.

ZIKAction: http://zikaction.org/
Led by PENTA, the ZIKAction research consortium brings together 14 partners across South and Central America, the Caribbean and Europe with the complementary goals of 1) developing a multidisciplinary multinational ready-to-act network capable of rapidly addressing any maternal and paediatric research need arising from (re-)emerging infectious diseases including Zika virus and 2) conducting an interdisciplinary programme of research studies within this network to address key knowledge gaps relating to ZIKV epidemiology, natural history and pathogenesis, with a particular emphasis on maternal and child health. ZIKAction is funded by the European Union’s Horizon 2020 Programme. ZIKAction works closely with two other European Union-funded consortia, ZikaPLAN and ZIKAlliance, to establish a Latin American and Caribbean network. This network will address the broader issue of building local capacity in Latin America to prepare for and rapidly launch a large-scale research response to emerging infectious disease threats. The three consortia also have common bodies for the global management of scientific programs, communication, and ethical, regulatory and legal issues.

c4c: https://conect4children.org
Coordinated by PENTA, c4c aims to improve the feasibility and impact of the overall paediatric medicines research agenda, providing crucial information at the right time for the licensing and use of medicines in children by a) generalizing and harmonizing existing good practice; b) basing trial design on feasibility, clinical expertise and well-justified selection of contemporary methodology; c) working with industry, public funders and regulators in a partnership that is based on consistent delivery of high quality data and early engagement of all stakeholders in paediatric drug development and c) integrating children, young people and their families’ perspectives and needs
into the process. This initiative will benefit individual clinical study sites and national coordinating centres, providing harmonized, streamlined procedures across the trial lifecycle, access to a wide range of study sponsors through a transparent, evidence-based, network-wide vetting procedure, and input from relevant specialty networks and key opinion leaders on study design, implementation and assessment. Early and clearly coordinated communication between investigators and sponsors, regulators, and experts will streamline and facilitate the process of generating and applying much needed information on medicines for children.

**ECRAID-Plan (www.ecraid.eu)**

Building on the foundations of the European consortia COMBACTE and PREPARE, ECRAID aims to advance clinical research in the field of infectious disease by further organizing and developing a European clinical research network. The network will function as the backbone of clinical research activities, providing an efficient infrastructure capable to perform all clinical trial aspects, from study design to scientific publication. All activities will be coordinated by a lean, centralized organization allowing easy access for all relevant stakeholders. The current ECRAID-Plan project is a two-year H2020 funded project (January 2019-Dec 2020) that will develop the business plan for ECRAID. ECRAID is aiming to launch its operations by the end of 2020.

**Description of significant infrastructure, relevant to RECOVER**

PENTA coordinates a large European network of paediatric hospitals and ER where children with nCoV will be admitted and followed up according to the planned protocols. These centers have been already activated as part of PREPARE response Mode 2.
PARTNER 10: INSTITUT PASTEUR SHANGHAI (IPS)

Description of participant and main tasks

Institut Pasteur of Shanghai, Chinese Academy of Sciences (IPS) is a legally independent research institution among 26 life science institutes of Chinese Academy of Sciences (CAS). Established in the year of 2004, IPS is dedicated to enhance the preparedness and responsiveness to infectious diseases through cutting-edge research and sustained translation of solutions. IPS is now a member of Institut Pasteur International Network (IPIN), which constitutes 33 research institutes located in 26 countries on 5 continents.

Administered under the leadership of Chinese Academy of Sciences and the Institut Pasteur, IPS has synergized the resources and expertise of the two parties to emerge as a research powerhouse and technology provider in the field of infectious diseases of the country. Since its inception, IPS has evolved three interdisciplinary research programs covering pathogen biology, infection and immunity, vaccinology and immune therapy. IPS performs fundamental research on infectious diseases with unmet medical needs, including AIDS, drug-resistant pulmonary tuberculosis, viral hepatitis, oncogenic viral infections, fungal and parasite infections. IPS has also become an important and proactive taskforce among CAS and IPIN in fighting emerging and reemerging infectious diseases, from highly pathogenic influenza virus to Zika virus. Notably, some of the novel findings have led not only to excellent publications but also to patents with a great potential to the development of treatment or prevention. An indicator of this progress is the increasing interest of domestic and global biotech companies to establish partnerships with IPS.

In 2016, the innovation capability for science and technology of the Institute continued to increase. IPS had 138 projects (including 36 newly commenced), 33 patents, and 89 published papers. The Institute's basic and applied research teams were complementary and coordinated, and they made remarkable technology transfer achievements in the field of infectious diseases. IPS signed over 20 technology transfer agreements including know-how transfers, patent licensing, technology trade-in investments and cooperation developments. The total contract amount reached 100 million RMB.

Currently, there are 23 principal investigators recruited from French and other international scientists among 138 employees. About 215 graduate students and post-doctorates are enrolled and studying in IPS, including 18 international students and post-doctorates (9 French students and post-doctorates). IPS provides a state-of-the-art research facility in the brand new 160,000 sf. research tower on the campus of Shanghai Institutes of Biological Sciences (SIBS) of CAS.

To contribute more to the global preparedness and responsiveness to infectious diseases, IPS start to work closely with both CAS and IPIN member institutes, to address the grand challenge of public health in the regions along the "One Belt & One Road" countries. Joint efforts have been implemented on pathogen discovery and solutions to disease control and prevention. IPIN members in Senegal and Cambodia are collaborating with IPS to develop kits for quick diagnostics, to screen and develop drug candidates and protective antibodies, to design and test various much needed vaccines.

Hefei CAS-Affiliated Hospital n°1 is located in the Anhui provincial capital Hefei. The infection disease unit of the hospital will provide clinical samples they have stored previously and are receiving daily, provide onsite testing/validation of diagnostic kits designed by IPS and other CAS institutions, collaborate with IPS to isolate nCoV at the P3 lab annexed to Anhui CDC, to conduct viral/cellular/pharmacological studies proposed by IPS and other CAS institutions and collaborate with IPS in translational studies, with patients in treatment, on molecular epidemiology, causal/effect correlation of susceptibility, morbidity/mortality and so on.
Profiles of main persons involved

**Prof. Fernando Arenzana-Seisdedos (m):** Corresponding IPS scientist for RECOVER. IPS scientific advisory director. MD, University of Sevilla (Sain), specialist in Pediatrics and Doctor in residency at the Pediatric Immunology and Rhumatology Unit, Hospital Necker Enfants-Malades. INSERM and Institut Pasteur staff scientist. From 2007 to 2016, he was the head of INSERM and Institut Pasteur research units. Since 2016, he is the scientific co-director at Institut Pasteur Shanghai/Chinese Academy of Sciences. He was the director of scientific careers at Institut Pasteur (Paris) (2007-2009) and president of Pasteur/Weimann Scientific Council (2011-2014). He is a scientific advisor to research institutions in Spain (IDIBAPS, Hospital Clinic, Barcelona) and Institut Pasteur International Network (IP Dakar), and a member of the Bettencourt-Schueller scientific council. His scientific research activities focus on immunology and virology (transcriptional regulation of HIV-1 replication; mechanisms of viral entry HIV and Flaviviruses). Prof. Arenzana’s major scientific contributions are 1) HIV transcription regulation in antigen specific T CD4 lymphocytes (PNAS 1990), 2) Mechanisms of HIV-enhancer regulation in primary T cells (EMBO J 1995), 3) identification of SDF-1/CXCL12 as the natural ligand of major HIV-1 coreceptor CXCR4 (Nature 1996a) 3) first description mechanisms of interference on HIV entry by HIV-1 coreceptor natural ligand (CXCR4- SDF1/CXCL12) and CCR5 chemokine-derived antagonists (J Exp Med 1997, Nature 1996b) 4) DC-SIGN as attachment molecule involved in viral entry (Immunity 2002, EMBO Reports 2003). Citations: 26122, h index:73, i10 index:120. (Google Scholar)

**Prof.. Hong Tang (m).** Director General of Institut Pasteur of Shanghai, Chinese Academy of Sciences from the end of 2015, received his BSc of Biochemistry from Nanjing University (1988), PhD in Molecular Genetics and Microbiology from Rutgers University-Waksman Institute of Microbiology (1996). He finished postdoctoral research on molecular immunology in Massachusetts Institute of Technology-Center for Cancer Research with Dr. Phillip A. Sharp (1996-1999). He was then a Postdoctoral Fellow of Irvington Institute for Medical Science Foundation. He then after was employed as a senior scientist in Dupont Pharmaceuticals Cancer & Genetics Department (2000), before returning to China. He set up the first Center for Molecular Immunology in CAS history. In 2012, he was selected by CAS as Deputy Director General of Wuhan Institute of Virology (2012), to strengthen the research and development of countermeasures of major infectious diseases. Dr. Tang has been serving on several important committees, including Infectious Diseases Review Panel (2007-2015) of State Basic Research Development Program of China (MOST 973), Strategic Review Panel for National Programs of Prevention and Control of Primary Infectious Diseases of Viral Hepatitis and AIDS (2008-2012), and SARS Task Force on Science and Technology of MOST (2003). He helped to discover the new paradigm of immune pathogenesis by the highly pathogenic coronavirus in mice, and possess scientific and administrative skills to coordinate a large-scale clinical studies of SARS cohorts.

**Prof. Dimitri Lavillette (m):** Dimitri Lavillette received his PhD in 2000 in Lyon (Lyon University) and achieved a 3 year post doc in the laboratory of David Kabat (“HIV-1, retroviruses and receptors”; Portland, Oregon, U.S.A.). He then secured a tenure staff scientist position at the National Center of Scientific Research in France (CNRS) (2003-2014). In 2014, he took a Professor position at the Pasteur Institute Shanghai – Chinese academy of Sciences (IPS-CAS, China) to animate the “Interspecies transmission of arboviruses and antiviral therapies” focusing on emerging and re-emerging viruses transmitted by mosquitoes like Dengue and Chikungunya viruses. He worked on major virus threats including SARS CoV. He masters the molecular virology and he generated different strategies to establish cDNA molecular clones, replicons and retrovirus pseudotypes. He is an entry specialist and developed neutralizing assays. He can easily dissect mechanism of neutralization of antibodies with different tools.

**Prof. Lubin Jiang (m):** Jiang Lubin is a Professor of Pathogen-Host Interaction and Epigenetics at the Institut Pasteur of Shanghai(IP), Chinese Academy of Sciences (CAS), Shanghai of China. He received his B.Sc. degree in Biology and M.S. degree in Botany from Nanchang University, Ph.D. degree in Genetics from Shanghai Institute of Plant Physiology and Ecology, CAS, in 1996, 1999, and 2003, respectively. He had held visiting post-doctoral fellow and research fellow positions at the National Institutes of Health, US before joining the IPS, CAS. His research interest centers on the molecular mechanisms and biological consequences of epigenetic and genetic factors of pathogen and host interaction in major infectious diseases, such as HIV, severe malaria caused by Plasmodium falciparum, with the long-term view toward the design of novel drugs, vaccines and diagnosis. He was awarded the Performance 32
Prize by NIH in 2010 and was selected as One Hundred Talents in CAS in 2013. He has also served as a reviewer for the international journals of PLOS Pathogens, Malaria Journal, PLOS One, etc. Lubin Jiang’s research interests center on understanding the molecular basis of the epigenetic regulatory mechanisms of P. falciparum genes and their applications in development of novel antimalarial drugs and malaria vaccines. Recently, his unit has screened broadly neutralizing antibodies against malaria and 2019-nCoV.

Prof. Xiaoming Zhang (m) obtained his PhD of Immunology at the University Pierre et Marie Curie in Paris in 2007, and pursued his post-doctoral fellow position at the Institut Pasteur from 2007 to 2012. He then became Principal Investigator at the Institut Pasteur of Shanghai where he leads the Unit of Innate Defense and Immune Modulation since 2012. His unit research projects consist of the 1) human B cell biology and antibody response in health and disease; 2) monoclonal antibody and engineering; and 3) deep immune profiling by scRNAseq, high-dimensional flow cytometry and multi-color immunohistochemistry.

Prof. Gary Wong (m) received his PhD in Medical Microbiology in 2014 from the University of Manitoba, in which his work focused on the development and characterization of vaccines and antivirals against Ebola virus, as well as immune responses important with protection. He is now a Principal Investigator at the Institut Pasteur of Shanghai, where his current research interests include 1) the establishment of rapid, sensitive and specific methods for on-site diagnostics, 2) the development of animal models, vaccines and therapeutics, 3) mechanisms of pathogenicity for Biosafety Level (BSL) -3 or -4 viruses causing viral haemorrhagic fevers in humans, with focus on bunyaviruses, and 4) viral pathogen discovery and characterization, specifically those with zoonotic origins in the Greater Mekong Subregion. His most significant research contributions include the development and characterization of vaccines (VSVΔG/EBOVGP) and therapeutics (ZMapp) against filoviruses, such as Ebola virus (EBOV), where he showed that vaccination with VSVΔG/EBOVGP can provide long-term immunity, and mechanistically protects via the induction of IgG antibodies.

Prof. Jie Cui (m) received his PhD in Ecology in 2011 from the East China Normal University, majoring in viral ecology and evolution. He is now a Principal Investigator at the Institut Pasteur of Shanghai, and group leader for Unit of Pathogen Bioinformatics. He has 51 peer-reviewed publications. His work focuses on evolution of emerging infectious diseases and big data analysis for pathogen induced cancer and other diseases. Most significantly, 1) he solved the early evolution of SARS-CoVs; 2) established the first bioinformatic pipeline for pan-avian endogenous viruses; 3) deciphered the early evolutionary pattern of 2019-nCoVs in China.

Prof. Hao Pei (f) is in charge of the bio is in charge of the bioinformatics platform of Institute Pasteur of Shanghai. In the past ten years, Prof. Pei was focused on methods of bioinformatics research, construction and system biology and bioinformatics platform tools of omics studies. Relying on solid fundamentals of applied mathematics, computer sciences and experience in large-scale software development platform, she conducted fruitful research in the field of Bioinformatics and has achieved some success. She has developed a series of methods for the multidimensional omics-data analysis and their applications. Current research activities focus on ii) development of new algorithm for the molecular evolutionary analysis of virus, the network modelling of viral pathogenicity, and the molecular dynamics simulations to evaluate the spread of the virus in the host, iii) construction of multiple bioinformatics platforms for virus detection, prevention and evaluation of drug resistant mutations. iiii) addressing the challenge of big data in life science,

Prof. Nicolas Berthet (m) obtained his PharmD in 2003 at the University of Grenoble and PhD in 2007 at the University of Denis Diderot. He then attended systematic virology and genome analysis trainings at the Institut Pasteur and “NGS and Cancer” training at the Canceropole in Paris. In 2013, he joined CIRMF (Gabon) where he was in charge of both a research unit on emerging viruses in Africa and a high-throughput sequencing platform dedicated to the molecular characterization of pathogens. After the Gabon, he joined the Institut Pasteur of Shanghai in 2019 where he set up his unit of Discovery and Molecular Characterization of Pathogens. His lab mainly focuses on i) discovery and molecular characterization of pathogens from primary samples based on the use of different high throughput sequencing technologies, 2) the prognostic markers to anticipate the progression of precancerous lesions to malignancy for cervical cancer and 3) the various high-throughput sequencing technologies for bacterial and/or viral metagenomic research projects.
**RECOVER**

**Prof. Huang Zhong** (m) is a Principal Investigator at the Institut Pasteur of Shanghai where he is head of the Vaccinology and Antiviral Strategies Research Unit. His laboratory has broad interests in developing vaccines and antiviral drugs for major viruses of interest in public health, including enterovirus 71 (EV71), coxsackievirus A16 (CVA16), hepatitis C virus (HCV), and HIV. Currently, they are focused on creating virus-like particle (VLP)-based novel recombinant vaccines.

**Professor Xu Tao** (m) received his bachelor's and doctoral degrees from Huazhong University of Science and Technology; from 1996 to 1999 he worked as a postdoctoral researcher at the Max-Planck Institute for Biophysical Chemistry in Germany; returned to China in June 2000 as a life science and Director and Deputy Dean of the Institute of Biophysics and Biochemistry of the Institute of Technology. In the same year, he was hired as a Distinguished Professor of the Yangtze River Scholars Reward Program. In the same year, he was funded by the National Science Foundation for Outstanding Young People. Work of the Institute of Biophysics of the Chinese Academy of Sciences; Director of the Institute of Biophysics of the Chinese Academy of Sciences and director of the State Key Laboratory of Biomacromolecules in 2007; In 2017, he was elected as the vice chairman of the first board of the Chinese Academy of Sciences Fellows of Foreign Students, and in the same year was elected as an academician of the Chinese Academy of Sciences; in 2018, he was elected as an academician of the Academy of Sciences of the Developing Countries. He is mainly engaged in the research of islet \( \beta \) cell function and cell biophysical technology.

**Professor JianPing Weng** (m). Professor of the Department of Endocrinology. Executive President Hefei CAS-affiliated Hospital n°1. His research interests focus on endocrinology, metabolic disease and genetics in diabetes. He has published over 100 scientific articles in international peer-reviewed journals including the Lancet, Molecular Endocrinology, Endocrinology, Human Genetics, Diabetes, Diabetes Care. He is the Editor-in-Chief of the Chinese Journal of Diabetes Mellitus, and the Associate Editor-in-Chief of the Chinese Medical Journal. Dr Weng was the President of the Chinese Diabetes Society 2012-2015

**Dr. Ma Xiaoling** (f). Member of the Inspection Branch of the Chinese Medical Association, a member of the Microbial Specialty Committee of the Inspection Branch of the Chinese Medical Association, chairman of the Anhui Medical Association's Laboratory Specialist Committee. Two major research lines: i) the antitumor effect of bacterial toxins, ii) bacterial adaptation and regulation mechanism.

**Selection of relevant publications**


**Relevant projects**

ZikAlliance: [https://zikalliance.tghn.org/](https://zikalliance.tghn.org/) IPS-CAS was the sole Chinese institute to integrate ZIKAlliance. This ZIKAlliance project is a multinational and multi-disciplinary research consortium comprised of 53 partners worldwide, funded by the European Union’s Horizon 2020 Research and Innovation Programme (see Partner 4; for full description of the project). IPS-CAS was part of the WP3 Virology and antivirals which aimed at providing crucial research and diagnostics tools to identify host factors involved in ZIKV control of infection and pathogenesis, as well as to identify drug and neutralizing antibodies. As part of the ZIKAlliance, IPS-CAS was eligible to apply
MOST matching fund and obtained it (2016YFE0133500). The MOST grant aimed to prepare tools (viral antigens and antibodies) and develop mice models to study pathogenesis and test drugs or neutralizing antibodies. Scientists from IPS-CAS participate to annual meeting of ZIKAlliance in France and in Brazil, and reported data. IPS-CAS was also able to exchange reagents (viruses and antibodies) within the consortium, attesting that this institute is well integrated in international research system.

Description of significant infrastructure, relevant to RECOVER

Hefei CAS-affiliated Hospital n°1 has 6 specialized clinical centers, where Infectious Disease Unit is the focal site for WARD (Wuhan Acute Respiratory Disease) caused by nCoV. This Unit is one of the two clinics in charge of WARD in-patient and out-patient for entire Anhui Province (Anhui Province is now the third in terms of nCoV positive patients). It has 160 beds and right now 80 severe patients are treated on site. It receives every day (February 2020) around 100 out-patients for nCoV2019 diagnosis.
4.2 Third parties involved in the project (including the use of third party resources)

<table>
<thead>
<tr>
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<td>The Antwerp University Hospital (UZA) provides high-quality tertiary care, academic training and scientific research. The UZA microbiology laboratory is the hospital’s routine microbiology lab and is the Belgian reference lab for enterocci, β-hemolytic streptococci (non-group B) and respiratory viruses. UZA will house the central facility of over 30 freezers coupled to local hubs, one of which is stationed at LMM, UA. The SLIMS system, which is already functional at UZA, will also govern the entire UA-UZA biobank system documenting all sampling handling and a list of key sample data and is connected to a local database containing all scientific data.</td>
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The clinical studies in RECOVER will involve patient inclusions and sampling at primary care sites and hospital sites across Europe, drawn from the extensive clinical research networks of PREPARE and COMBACTE. The choice of clinical sites/networks will be made at the start of the project, based on sites readiness and willingness to participate. The selected clinical sites/networks will provide their resources in kind against payment to UMCU (Article 11). Once identified, the EU will be informed of the details of the third party clinical sites.
If yes, please describe the third party, the link of the participant to the third party, and describe and justify the foreseen tasks to be performed by the third party

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**AMC Medical Research B.V.:** Third party providing in-kind contributions to the Beneficiary Academisch Medisch Centrum bij de Universiteit van Amsterdam (AMC)/Third party with authorization to administer given by the Beneficiary Academisch Medisch Centrum bij de Universiteit van Amsterdam.

AMC Medical Research B.V. (AMR) is a non-profit SME owned by the AMC (the beneficiary). AMR was established in order to manage the financial, legal and administrative tasks of AMC in externally funded research projects, including EU funded research projects. Furthermore article 12 of the Grant Agreement is applicable. AMR makes its resources available (at no costs for the action) to AMC by employing temporary research personnel and handling the payment of travel, equipment, other goods and services. The resources are used on the premises of AMC and are under its direct responsibility. These will be direct costs for AMC assimilated as “own resources” charged to the action.

The costs of the resources charged to the project by the AMC are actual costs recorded in the accounts of AMC Medical Research B.V.

All of the above is based on the general agreement made between AMC and AMR for managing externally financed projects.

The resources made available by AMR to AMC are research personnel as allocated to AMC in the overall budget necessary for AMC to perform its designated tasks. The in kind contribution is used on the premises of the Beneficiary.

**General data**

**Beneficiary name:** AMC Medical Research B.V.
**Beneficiary address:** Meibergdreef 9/location J1a-229
**Postcode:** 1105 AZ
**City:** Amsterdam
**Country:** The Netherlands
**Telephone number:** +31 20 566 5558
**Fax:** +31 20 691 5462
**Website:** [http://www.amr.nl](http://www.amr.nl)
**e-mail:** secretariaat@amc.uva.nl

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| 9. PENTA |
|---|---|
| Does the participant plan to subcontract certain tasks (please note that core tasks of the project should not be sub-contracted) | N |
| If yes, please describe and justify the tasks to be subcontracted |
| Does the participant envisage that part of its work is performed by linked third parties | N |
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| Does the participant envisage the use of contributions in kind provided by third parties (Articles 11 and 12 of the General Model Grant Agreement) | N |

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<p>| 10. Institut Pasteur Shanghai (IPS) |</p>
<table>
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*IP Shanghai provides the laboratory research support for the Chinese Academy of Science Affiliated Hospital in Hefei, which is a designated centre for the case of patients infected with N CoV. Anhui province at present has 800 patients, and is expecting to see more given the local epidemiology at present, although stringent quarantine measures have been imposed, aiming to contain the spread of nCoV. We will explore together with IPS how the Hefei Hospital will contribute resources in kind to partner IPS.*
5. ETHICS AND SECURITY

5.1 Ethics
In the research proposed in RECOVER we identified the following ethical aspects as applicable:

- Research on Humans;
- Use of Personal Data;
- Research on Animals;

Research on Humans

General Ethics Policy

RECOVER, including its third parties and recruiting sites, will work under the central ethics policy as currently active under PREPARE, COMBACTE and VALUE-Dx, encompassing the following key elements:

All necessary ethical approvals and permits will be obtained prior to the start of the research activities in RECOVER. Ethical approval requests will encompass information on:

- Patient recruitment procedures, including number of participants, inclusion and exclusion criteria, the use of incentives, and patient risks versus patients benefits;
- The informed consent procedures.
- The data collection and sampling procedures (e.g. type of samples, amount, type of (personal) data);
- Patient feedback procedures;
- Data anonymization procedures;
- How the study deals with privacy/confidentiality aspects and the procedures and safeguards that will be put in place in data collection, storage, protection, retention and destruction;
- Restitution of the results of the studies to participants and national authorities;

Compliance with the applicable international, EU and national legislation and conventions in relation to: The conduct of human studies:

- Declaration of Helsinki (2013);
- Directive 2001/20/EC (Clinical Trials Directive),
- Regulation EU No 536/2014 (Clinical Trials Regulation),
- Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo Bioethics Convention);

The study and handling of biological materials:

- EU Directive 2004/23/EC on the quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells
- WHO Guidance on regulations for the Transport of Infectious Substances 2015-2016

Dataprotection and confidentiality:

Convention for the Protection of Individuals with regards to Automatic Processing of Personal Data (1985).
Recommendation No. R (97) 5 on the Protection of Medical Data (1997).
Declaration on Ethical Considerations Regarding Health Databases (2002).

Ethics management
Ethics management fall under the responsibility of WP1. The Executive Board (EB) operates as the central Ethics management body that is responsible for implementing the Ethics policy. All partners in RECOVER are highly experienced in the design and execution of the proposed research studies. They are aware of all ethical requirements and processes involved and have the systems and procedures in place needed to monitor compliance to all relevant ethical and regulatory requirements. As part of the regular WP reports (see section 3.2) all partners will report on a regular basis the obtaining of all relevant ethical approvals. The sponsor(s) of the clinical studies will collect all approvals from the recruiting sites. Copies of ethical approvals can be made available to the European Commission’s services upon request. Experience and track record in ethical approval processes will be part of the site selection process for the clinical studies. If and when needed, the EB will seek advice on ethical issues specific to RECOVER from the ethics experts.

In the international transport and storage of clinical samples, applicants confirm to comply with the Oviedo convention (Convention on Human Rights and Biomedicine - CETS 164, http://www.coe.int/t/dg3/healthbioethic/Activities/01_Oviedo%20Convention/default_en.asp) and the Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin (Adopted by the Committee of Ministers on 15 March 2006 at the 958th meeting of the Ministers' Deputies) https://wcd.coe.int/wcd/ViewDoc.jsp?id=977859.

RECOVER partners confirm that research conducted outside the EU is legal in at least one EU Member State. No materials will be imported to/exported from EU.

Details on the incidental finding policy will be provided by RECOVER's Executive Board in the early stages of the project.

Informed consent
A standardised approach to obtaining and documenting informed consent with central record management will be used. A standardised Informed Consent Form (ICF) will be used in the clinical studies with study and jurisdiction modifications, as required. In brief, the ICF will include a clear explanation of the aims, methods, objectives and potential hazards of the study. The ICF will also make clear that patients are completely free to decline to answer any questions, decline to enter the study or to withdraw from it at any time, for any reason. Participating or not in the RECOVER studies will not affect the care received by the individual. Potential dependency will be resolved by emphasising the voluntariness of participation and, as much as possible, separation between clinical and research roles. The research analysis of human samples and/or medical information will occur only after provision of specific information and explicit consent for these research activities. The ICF will include details of how samples and data will be handled at the end of RECOVER or in the event that a patient withdraws consent. Indemnity provisions will also be clearly stated in the ICF. The ICF will inform study participants that they have the right:

- To know that participation is voluntary.
- To ask questions and receive understandable answers before making a decision.
- To know the degree of risk and burden involved in participation.
- To know if there are any benefits involved in participation.
- To know the procedures that will be implemented in the case of incidental findings.
- To receive assurances that appropriate insurance cover is in place.
- To withdraw themselves and their samples and data from the project at any time.
- To know how their biological samples and data will be collected, protected during the project and either destroyed or reused at the end of the research.
- If plans to re-use the data exist, participants should be duly informed, and consented also for this further usage.
- To know of any potential commercial exploitation of the research.
Furthermore, as the RECOVER studies will potentially include the enrolment of children and those lacking in capacity we will design next of kin / person responsible / legally authorised representative ICFs to allow recruitment of these patients. Enrolment of children and those lacking in capacity is essential to obtain insight into the main determinants of transmission of SARS-COV-2. After all, at the current stage, it is unclear what role children play in the spread of the virus. The clinical study teams will include experts in the conduct of clinical research in children, lay persons and ethicists who will ensure that all studies involving children and their consent process reflect the best interest of these participants. The ICF and patient information sheets will be submitted to local Ethics Review Boards before the commencement of the study in accordance with local regulations. No remuneration will be offered for participation in clinical studies and particular care will be taken to ensure that consent is given freely and without coercion according to the Principles of ICH-GCP, the Declaration of Helsinki 2008, the Human Tissue Act (2004) and Human Rights Act (1998). This is made clear in the consent forms used.

Principle investigators running the studies will ensure that patient involvement does not cost volunteers or patients money, i.e. reasonable travel costs will be paid and there will be no cost to the individual, their private medical insurance (if any), or the public health insurance plan for the study procedures. Study treatments will be provided free of charge for the duration of the study. No invasive physical procedures will be used.

**Human samples handling**

For the type of samples to be collected we refer to the enclosed clinical study template. When samples are collected, the investigators staff members must ensure that samples are collected with informed consent and ethics committee/ Institutional Review Board (IRB) approval in accordance with the applicable research requirements of Good Clinical Practice (International Conference on Harmonisation) and applicable local regulation. Consents and information sheets will be generated, and local approval gained prior to the commencement of any studies. When an investigator obtains samples from a source where the collected sample was made for reasons unrelated to the project, or uses retrospectively collected samples, the relevant investigators staff members must ensure provide and retain evidence that the entity complied with relevant requirements for informed consent, ethics committee/IRB approval and data privacy. No sample will be used in RECOVER without this evidence being available. RECOVER will not utilise samples that are collected for reasons unrelated to the project unless prior written approval of the Ethics Committee is obtained. In general, derivatives (e.g. isolated proteins) and preparations of human biological materials (e.g. sub-cellular fractions and bacterial isolates) that are well established and made available for research use, do not require re-consent and/or ethics committee/IRB approval for the intended research use. Investigators will need to make a case-by-case analysis, in order to determine whether consent is required or not.

At the end of the project provision will be made to keep the samples within the bio-bank or dispose as appropriate. Where respiratory samples are taken, leftover portions of samples will be shipped to central laboratory at Partner 1 UA for validation of test accuracy and other purposes.

If the samples are known to contain a highly pathogenic organism, the experiments will be performed in laboratories equipped with class II safety cabinets or higher as appropriate for the organism and route of infection. The laboratory sites will be responsible for ensuring that strict safety procedures and correct personal protective equipment are available for use by the laboratory member. No genetic modification will be performed on the organisms and no stock piling of any agent will occur. All laboratory and clinical staff have a long track record in and are trained to work with the samples collected as part of the clinical studies.

All samples will be processed, transported and stored according to strict standard operation procedures. All of the biomaterials will be stored in the biobank. The RECOVER principal investigators and the recruitment sites will write a uniform ethics application that will be submitted to the local ethics protection authorities as part of the overall ethics applications for the clinical studies. The sample specific data will be kept in the central repository under the supervision of Partner UMCU.

Material Transport Agreements as have been used in PREPARE between the partners will be prepared for the transport of samples. In addition, we will use the PREPARE/ COMBACTE protocols for the collection, packaging and shipment of diagnostic samples in accordance with international guidelines and regulations should the need arise to send samples for bio-banking or additional tests within the network. The International Air Transport Association regulations will be followed with an IATA qualified technician packing the samples. Only an approved courier will carry the samples following IATA protocols. If the sample is known to contain a category A infectious substance (UN2814), the safety offices of the institutions involved will be included in the discussions on sample
Use of personal data

The research in RECOVER will involve the collection of “Personal Data”, defined as “any information, private or professional, which relates to an identified or identifiable natural person” in Article 2(a) of EU Directive 95/46/EC.

This includes:
- Demographic details including: age, gender, smoking status and co-morbidities (cardiovascular disease, lung disease (COPD/asthma), diabetes, other chronic condition, vaccination status);
- Duration of symptoms prior to consulting;
- Presence of selected symptoms and severity rating of each symptom;
- Recorded or body temperature;
- All tests done or ordered;
- Antibiotic prescription (class, dose duration);
- Additional prescribed medicines;
- Working diagnosis (subcategory of severe respiratory disease, e.g., URTI, Exacerbation of COPD, Bronchitis, pneumonia);
- Suspected aetiology;
- Advice about over the counter and symptomatic medicine use;
- Advice about taking time off work or school;
- Setting;
- Cost data;

The research will NOT involve:
- Collecting and processing data which is not necessary for the purpose of the study (see Separate Clinical Research Template).
- Collecting sensitive personal data on sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction.
- Processing any human genetic information.
- Secondary use of data (defined as further processing of previously collected personal data including use of pre-existing data sets or sources, merging existing data sets, sharing data with non-EU member states);
- Tracking or observation of participants (e.g. surveillance or localization data, and Wan data, such as IP address, MACs, cookies etc.)

As mentioned in this section, we confirm that we will only collect and process relevant data, guarantee data anonymization and prevent unauthorized access to personal data. In the early stage of the project, we will provide a more detailed description of the anonymization technique and of the security measure that will be implemented to prevent unauthorized access to personal data. In addition, we will further explain how all of the data we will process is relevant and limited to the purposes of the research project.

General Principles for handling human data in RECOVER

Personal identifiable information (PII) collected in RECOVER will be processed in compliance with relevant legislation and guidance, and applicable international, EU and national law, specifically the new General Data Protection Regulation No 2016/679 as of from 25 May 2018.

The principles contained in the World Medical Association Declaration of Helsinki on the Ethical Principles for Medical Research Involving Human Subjects (2008) will be strictly adhered to. In general terms the appropriate data protection principles will be observed, including:
- Data are fairly and lawfully processed;
- Data are used only in ways that are compatible with the original consent;
- The amount of data collected is relevant and not excessive;
- All reasonable efforts are taken to ensure data accuracy;
- The data are used in accordance with the rights of the study participant;
- The data are stored securely;
- The relevant international and national guidance will be consulted.
The trial staff will ensure that the participants’ anonymity is maintained. Only anonymised patient data will be captured on the CRF, sample tubes and any electronic database. Unique study identifiers (Subject ID) will be used to identify the subjects in the eCRF database. Local teams will log patient identifiable data (like name, contact data and date of birth) in a separate data source to link the subject to the correct Subject ID number. These data sources, that are only accessible for the local authorised trial staff, are stored at a secured location on site. This prevents that a direct link can be established between personally identifiable data and clinical research data in the central database. Anonymised clinical trial data will be captured using Research Online, which is also used in PREPARE, COMBACTE and VALUE-Dx. This data management system meets all GCP guidelines for electronic data collection in terms of protecting data integrity and securing the information collected. This means, among other things, that users will get a role based access to the system after they have logged-in using their own username and password. The role based access to the system will avoid unauthorised data access and prevents that users perform actions that they are not allowed to do. Furthermore, the system has an extensive electronic audit trail that will log all data entry steps with timestamps, update reasons and user information. Data entered into the system will be transferred over the internet with secured encrypted data communication using the Secure Socket Layer cryptographic protocol. Submitted data will be stored immediate and automatic in cloud based databases which are hosted in a ISO/IEC 27001:2013 certified data center located in the European Union (Amsterdam).

Use of Animal Models

Description of animal use
RECover will use in laboratory animals for immunisation studies in WP5. At Erasmus MC all animal experiments will comply with the Dutch Law on Animal Experiments (Wod, ID number BWBR0003082) and will be approved by independent Animal Ethics Committees. To minimize animal suffering, a minimum number of animals will be used that allows us to demonstrate statistical significance of results. The animals will be humanely euthanized when predefined humane endpoints are reached. Erasmus MC certifies that they will adhere strictly to all existing ethical and safety provisions of the EU. Animal experimentation will fully implement the 3Rs policy (Refinement, Reduction, Replacement) within the project. They will make every effort to reduce pain, distress or other adverse effects leading to suffering of the animals and to enhance animal welfare (Refinement). The number of animals used in the project will be kept to a strict minimum while still ensuring that statistically valid results are produced. This will be achieved through sharing of samples and materials as well as close collaborations and discussions amongst partners (Reduction). The transmission of viruses can only be determined by animal experimentation; therefore a Replacement by in vitro studies is not possible.

Animal experiments using ferrets will be performed according to the guidelines from the Institutional Animal Welfare Committee (protocol no. AVD1010020174312, approved 5-7-2018). The studies will be performed under biosafety level 3 (BSL3) conditions. To study 2019-nCoV transmission, a modified version of the previously described influenza A virus ferret transmission set-up will be used. With this set-up virus transmission can be studied best under experimental conditions. This set-up consists of two clear polymethyl methacrylate cages of different sizes. Donor ferrets and direct contact recipients will be housed in a cage of 35 cm × 30 cm × 65 cm (W × H × L), whereas airborne recipients will be housed in a cage of 30 cm × 30 cm × 55 cm (W × H × L). These cages are separated by two stainless steel grids 10 cm apart to prevent direct contact but still allow airflow from the donor ferret to the airborne recipient ferret. These transmission cages allow the experiment to be conducted in negatively pressured isolators in the BSL3 facility, with HEPA-filtered airflow <0.1 m/s. Both male and female ferrets with an age range of 6 months–2 years in these experiments. For a virus transmission experiment, twelve ferrets will be randomly distributed into four individually housed groups to assess transmission of one virus isolate (e.g. 2019-nCoV or SARS-CoV). In total 4 different viruses will be studied, resulting in the expected use of 48 animals. One naïve ferret from each group will be inoculated intranasally with 0.5 mL of 1 × 105 TCID50/mL 2019-nCoV (250 µL per nostril), thus acting as donor ferrets. The other two ferrets will be used as direct contact and airborne recipients, respectively. Donor and direct contact animals are of the same sex. All animals will be sacrificed at 14 days post exposure and blood will be collected to assess seroconversion.
Application of the three “R”s

RECOVER partners are aware that animal welfare is an important public concern and will therefore put strong effort in replacing, reducing and refining animal use, referred to as the 3R principles, if and when deciding to include animal studies.

Replace
While it would be desirable to exclude animals as a whole, the realization of the objectives of RECOVER requires the use of experimental animals. As mentioned above, no use of animals will be made in RECOVER for those research questions where adequate alternatives are available.

Reduce
The research groups will strongly engage to use the minimal number of animals needed to obtain scientific and statistical sound results. Therefore, the Beneficiaries involved in animal testing will be obliged to:

› Generate a document describing the procedures for animal testing in compliance with EU regulations (ETS No. 123 – European convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes)
› Perform a thorough statistical analysis to ensure that the appropriate number of animals is used to obtain sound and significant results. If no expertise on statistics is available at the institution, an expert will be consulted.
› Submit the completed documents, including the statistical analysis, to the local Ethical Committees of their institution.
› Make sure that animal experiments are not initiated before the appropriate Ethical Committee provided its approval. All Ethical Committee approvals will be collected and forwarded to the EC upon request.
› By strictly adhering to these procedures, non-interpretable results and, consequently, unnecessary repeats of animal studies will be kept to an absolute minimum. Where necessary, the conduct of small pilot studies will be used to consolidate experimental design, i.e., to establish challenge dose and avoid the use of larger numbers of animals in the main studies.

Refine
Besides reducing the number of animals, RECOVER partners using animals for their research will make every effort to alleviate or minimize pain, distress or other adverse effects suffered by the animals involved and to enhance animal well-being. Following measures will be or have been taken to fulfil this goal:

› Only Beneficiaries that have a longstanding and broad experience in working with animals, hold the necessary licenses from their local governmental agency and the local animal welfare commissioner to perform animal testing and comply with local legislation for conducting procedures on animals with welfare as the primary concern will perform animal studies in RECOVER.
› Throughout the animal studies, pain, suffering and distress will be alleviated or minimized unless it cannot be avoided based on sound scientific arguments. The latter will be defined by, and compliant with the local legislation.
› An objective scoring system will be used to continuously monitor pain, distress and discomfort throughout the study and to determine Humane End Points.
› When experimental procedures require analgesia or anesthesia, approved methods will be used such as described in “Laboratory animal anaesthesia – a practical introduction for research workers and technicians” (Flecknell, 1996) or similar approved references.
› When Humane End Points are reached or when experimental procedures are terminal, approved methods of killing will be used as described in “Recommendations for euthanasia of experimental animals – part 1 and 2” (Laboratory Animals, 1996 and 1997), “AVMA guidelines on euthanasia” (American Veterinary Association, 2007) or similar approved references.

The animal experiments do not include any deliberate release of infectious or genetically modified organisms during the course of the project and the material in contact with infectious or genetically modified agents will be sterilised before disposal from containment areas to prevent accidental transmission to the environment. We will implement
appropriate procedures to ensure full compliance with the Revised Directive 2010/631/EU on the Protection of Animals used for Scientific Purposes which became law in Jan 2013. During Project Agreement negotiations documentation will be collected and reviewed to ensure that all partners have all required documentation and infrastructure in place to adhere to these core principles. In all cases, experiments will be designed to use the minimum number of animals whilst retaining the power to give meaningful results. The numbers of animals required in each experiment will be driven by statistical power calculations based on data from previous studies and will be constantly reviewed based on ongoing data generation to ensure that optimum group sizes are used throughout the duration of the project. Study designs will be reviewed by the RECOVER principal investigators and also through local or national ethical review process, according to the national legislations.

5.2 Security
RECOVER will not involve activities or results raising security issues:
- activities or results raising security issues: (YES/NO)
- 'EU-classified information' as background or results: (YES/NO)

6. DATA SHARING

In conformance with Article 29.3 (option c) we will make available research data, at the latest within 30 days after it has been generated, through open access or, if agreed by the Commission, by giving access rights to those third parties that need the research data to address the public health emergency. Quality-controlled data will be shared in accordance with the FAIR principles.

A draft data management plan (DMP) is described below:

Introduction
This draft Data Management Plan (DMP) describes the (draft) requirements to develop and implement all data management related tools and processes and procedures of RECOVER. The DMP is developed based on the RECOVER proposal and the specifications obtained during the initial information gathering and analysis process. The DMP will serve as the basis for all further data management related activities within RECOVER. A more detailed full DMP will be developed during the first 6 months of the project.

The DMP will include: methodologies for data collection, data quality and standards, types of data, storage and curation, metadata standards, security and confidentiality, data sharing, data access and governance.

The DMP provides an explanation of the main elements of the data management policy that will be used by the beneficiaries with regard to all the datasets that will be generated by the project. Details that only apply to dedicated tasks will be documented in separate implementation plans (e.g.: specifications of CRF, electronic survey/questionnaire, reports, data mapping procedures, study logistic, data set delivery, data validation plan (DVP) and monitoring policy and timelines).

This first (draft) version of the DMP reflects the current knowledge of the data management related requirements for RECOVER and it is expected that during the conduct of the project these requirements will evolve and will lead to subsequent versions of the DMP.
RECOVER
RECOVER (Rapid European COVID-19 Emergency Research response) is a comprehensive research response to the SARS-CoV-2 outbreak addressing the most urgent questions for patient and public health level interventions. RECOVER originates from partners of the EU Framework 7 (FP7) funded PREPARE project (Platform for European Preparedness Against (Re-) emerging Epidemics). In RECOVER, we will address these urgent questions in a comprehensive, multidisciplinary and interacting set of research response activities, combing (i) clinical studies in primary and hospital care, (ii) epidemiological studies and modelling, and (iii) clinical biological studies. The proposed studies complement ongoing research in China, addressing key knowledge gaps and patient-cohort questions relevant to the European population. The research proposed includes essential needs for preparedness and response. RECOVER will inform future research response efforts to further strengthen Europe’s and global clinical research.

In doing so, RECOVER is organized into 6 Work Packages. All six WPs are highly interrelated, with most WPs interacting with most other WPs. WP2 (Primary Care), WP3 (Hospital care) and WP4 (Diagnostic/Lab support) are related to the clinical studies that will be carried out. WP5 will carry out biological studies whereas WP6 will be focused on transmission epidemic dynamics and modeling. The essential interactions and interrelationships between the WPs within RECOVER are depicted in the figure below:

Tasks related to the DMP

Data management tasks within RECOVER will be carried out to a large part by the Data Management department of the Julius Center (University Medical Center Utrecht) and will largely be built on the infrastructure already in place for the PREPARE and VALUE-Dx projects. Important data management tasks will be:
- The development of the enhanced Point Prevalence Audit Survey collection tool for WP2. The data collection tool (PPAS in Research Online) developed for the VALUE-Dx study will be
adapted to capture protocol adaptations of the enhanced PPAS.

- WP3 will take care of the expansion of the REMAP-CAP and MERMAID ARI 1.0 studies in the PREPARE consortium. The REMAP-CAP study will activate pandemic strata, modify the CRF to collect relevant data on COVID-19 and add additional sites and regions. The MERMAID ARI 1.0 study will be started up again using the same eCRF as was used in PREPARE.

- Within WP3 a new ARI 2.0 study will be implemented in Research Online to include all data and samples relevant for COVID-19.

- Another part of RECOVER WP3 is a survey to assess perceptions and preparedness of European healthcare workers for COVID-19. Results will provide guidelines handles on how to protect our healthcare personnel. Surveys will be send to hospitals in the network using CASTOR EDC.

- WP4 will send a survey among COMBACTE LAB-Net to access the capacity and capability to detect the new coronavirus. This survey will be send using the Combacte Network Management System (NMS) and Research Online.

- Studies will be conducted within households and health care workers to investigate transmission of the virus responsible for COVID-19 disease. Dedicated apps will be used to collect daily data.

**Data management systems in scope**

**Research Online**

The Electronic Data Capture system ‘Research Online’ will be used to implement the enhanced PPAS survey, the COMBACTE LAB-NET questionnaire, the REMAP-CAP study, the MERMAID ARI 1.0 study and the ARI 2.0 study. The EDC system guarantees a correct, complete and consistent data collection.

Data entry forms created in RO by the data manager can be easily accessed by all users (e.g. researchers monitors, study participant) using standard web browsers. Multiple validation and range checks will be programmed to assure complete and high quality data. Data that does not comply with these rules or ranges will generate a query that must be resolved immediately or at a later stage. Electronic workflows such as multiple skip and jump rules will ensure that only information that is applicable to the participating site will appear. After the data of last visit last subject is entered, the database can rapidly be closed and data managers will make data available for the researcher for further analysis and publication purpose.
Network Management System (NMS)
Within the NMS we will store contact information of the General Practitioners, Hospitals and Labs that participate within COMBACTE and VALUE-Dx. We will use the NMS to send out the LAB-NET questionnaire to access the capacity and capability to detect the new coronavirus of European labs. Collected information will be stored in Research Online.

RO and NMS are both developed and maintained by the data management department of the Julius Center and therefore it will be possible to develop new features in RO specific for the RECOVER project. This will be determined in close cooperation with the teams of WP2, WP3 and WP6 and other stakeholders.

SLIMS
The SLIMS system in Antwerp (WP4) will be used for sample management of samples collected within the ARI 2.0 trial (WP3) and samples collected within the enhanced PPAS (WP2). SLIMS will be used to register the collected samples and sample analyses test data. Furthermore SLIMS will also be used for bio banking purposes to register the location of the long term storage of the bio samples.
A direct interface will be realized between Research Online data collection and the SLIMS system to enable the direct and automatic registration of collected samples within SLIMS when this is indicated within the eCRF (RO). Furthermore the interface will send sample analyses data entered in SLIMS to the RECOVER Central Date Repository.

Castor EDC
The survey of WP3 to assess perceptions and preparedness of European healthcare workers for COVID-19 will be sent to hospitals in the network using CASTOR EDC.

Diary App
Dedicated apps will be used to collect daily data of the transmission studies of WP6. At this stage no further details of the apps are known. In subsequent DMP’s these apps, including the security and privacy measures taken will be described in detail.

RECOVER Central Data Repository
A RECOVER Central Data Repository (RECOVER-CDR) will be set-up within SQLserver using ETL processes and will be used to store as much data as possible of RECOVER. This means that data collected using the Research Online and SLIMS will be stored in this data repository. Also data from other external data sources may be stored in the DWH but this is not known at this stage. In subsequent DMP’s this will be described in detail.
Power BI
Data in the RECOVER-CDR is directly accessible by the business intelligence tool Power BI. Reports and visualizations related to study data will be created and made available to the relevant RECOVER users using Power BI.

Digital Research environment
Besides access to reports and visualizations, collected data will be made online accessible as well. Details are not known at this stage but probably an online Digital Research Environment (DRE) will be made available which will be based on the Azure cloud. Further details will become available during the conduct of the project.

Systems security

Research Online, Randomization Module and NMS
Generic for Research Online and NMS
Data from Research Online and NMS will be transferred over the internet using secured data communication protocols. All data will be stored automatically and regularly back-ups will make sure that data will never be lost. Databases and web servers of these systems will be hosted in a ISO/IEC 27001:2013 certified data center in the EU. Security is assured by ISAE 3402 type 2 and SOC 1 type 2 reports.

The servers are actively monitored (including memory, storage and CPU usage and network connections). When an incident occurs in the servers, the support desk is alerted and will resolve the issue.

In order to keep RO running smoothly, updates and fixes are required. Therefore server/database maintenance is scheduled outside office hours on a monthly basis in combination with a new software version. Any required scheduled downtime is limited to approximately 10 minutes. Major updates which require more than a 30 minute window will be planned and communicated to all involved study teams. Exceptions can be made for urgent security updates or issues that are causing high priority production issues.

A backup of all data (model and database) is made on a daily basis for the user acceptance testing and production environment. Backups are stored in secured locations that are geographically dispersed. The duration of storage is as follows:
- Nightly Backups: 2 weeks
- Sunday Backups: 3 months
- Monthly Backups (1st Sunday of each month): 1 year

Specific for Research Online
Besides these general security measures for RO, Randomisation and NMS there are additional measures for RO specific: This web based system meets all ICH-GCP, EMA (annex 11) and FDA (21CFR part 11) guidelines for electronic data collection in terms of protecting data integrity and securing the information collected. This means, among other things, that users will get role-based access to the system after they have logged-in using their own username and password. The system will log all data entry steps with timestamps, update reasons and user information. Role-based access to the system will avoid unauthorized data access and prevents users from taking actions for which they are not authorized.

Development
RO and NMS are all developed in MENDIX. This state of the art development platform enables very flexible and fast development of new functionalities to the system. A full DTAP (Development, Test, Acceptance, Production) approach is used in order to develop, test and deploy new releases of the software in a controlled way. An automatic test environment including hundreds of test cases is used for full regression testing of RO before new releases will be placed in to production environment.

SLIMS
SLIMS is an off the shelf application. This web based system meets all ICH-GCP, EMA (annex 11) and FDA (21CFR part 11) guidelines for electronic data collection and is implemented within the Central lab in Antwerp (WP4).
CASTOR EDC
CASTOR EDC is an off the shelf application. This web based meets all ICH-GCP, EMA (annex 11) and FDA (21CFR part 11) guidelines for electronic data collection and compliant to ISO27001.

RECOVER Central Data Repository
The RECOVER-CDR will be created using Microsoft SQLserver database. This database system resides within the institutional demilitarized zone of the UMCU. Authentication is provided by an on-premises Active Directory (AD). This AD is synchronized to the azure cloud by Azure AD Connect. Role based authorization (using AD groups) prevents unauthorized data access. Transport Layer Security (TLS) is in place for all connections from and to the Data warehouse Web server, Microsoft azure services and Mendix cloud applications. Web API calls to and from the Data Warehouse Environment are restricted to specific IP-ranges and open to certified clients only. Intrusion Prevention policies are in place to check for malicious activity and block/stop them if necessary. Data on our on-premises servers are regularly backed-up and all code is version controlled in Git. The backup rotation scheme for our databases is Daily-Weekly-Monthly-Yearly.

Power BI and Digital Research Environment
Both Power BI and DRE are applications residing in the Microsoft Azure cloud environment. Authentication is provided by an on-premises Active Directory (AD). This AD is synchronized to the azure cloud by Azure AD Connect. Role based authorization (using AD groups) prevents unauthorized data access. The Azure platform complies to over 90 certifications (see link: https://azure.microsoft.com/en-us/overview/trusted-cloud/compliance/).

Data collection using research Online

Designing PPAS survey and PRUDENCE eCRF in Research Online
The initial enhanced PPAS survey and the ARI 2.0 CRF will be defined in Word or Excel based on the study protocol. After all stakeholders agree on a (close to) final version of the survey or CRF data management will start with designing the eSurvey and eCRF within Research Online. When the eSurvey or eCRF has been designed by the data manager it should be tested by various stakeholders (eg Researcher, Project Manager, Monitor, Research nurse). Based on the feedback of the testing by the stakeholders the eSurvey and eCRF may be adapted until we have a final version. After signing of the final version of eSurvey and eCRF these will be taken into production.

Validation of data entry
Multiple validation checks will be programmed in the enhanced PPAS eSurvey and the ARI 2.0 eCRF to assure complete and high data quality:
• Required checks: if a question is required it must be answered, otherwise it is not possible to save the form.
• Ranges: the provided answer should be between the lower and upper range limits.
• Consistency checks: logical check between two or more questions (e.g. start date must be before stop date).
Beside these validation rules, multiple skip and jump rules will ensure that only information that is applicable to the patient will actually appear.

The PI or delegate will be responsible to define these validation rules, skip and jump rules in close cooperation with the Julius DM. The rules will be documented in a Data Validation Plan (DVP). Once the eCRF implementation is completed Julius DM will test the correct configuration of the validation, skip and jump rules against the DVP.

Workflow
It will be possible to define a workflow within Research Online to direct the data entry process. Using this workflow it can be defined at what point in time which eForms should be directed to which users. Workflows of the enhanced PPAS eSurvey and the ARI 2.0 eCRF are not know at this stage. In subsequent DMP’s this topic will be described in detail.
**User and site management**

DM will create the sites and user accounts needed for access to Research Online. Users will have role based access to the system after they have logged-in using their personal username and password.

In the table below there is an overview of which tasks can be performed with each type of account.

<table>
<thead>
<tr>
<th>Task</th>
<th>DM</th>
<th>Coordinator</th>
<th>Researcher</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log in into RO</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Create new study</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Create different entry groups</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Create sites</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Create new accounts</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assign accounts to sites</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Design forms</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Design workflow</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fill in data</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Print forms</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>View Reports</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Create queries</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respond to queries</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Close queries</td>
<td></td>
<td>X</td>
<td></td>
<td>X*</td>
</tr>
<tr>
<td>SDV</td>
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<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Lock forms</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signoff subjects</td>
<td></td>
<td></td>
<td></td>
<td>X**</td>
</tr>
<tr>
<td>Export study data #</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Optional

** Only if role 'sign' is given
# Only data on which account has access to
**Account requests**
Access will be granted to authorised representatives for the study only. The PI or delegate will request the creation and termination of the accounts by sending an email to the responsible data manager. At least the following user information is required:

- First and Last name
- Email address
- Site(s)
- Type of access (data entry or monitor)

An up to date list of users of Research Online including their respective roles will be maintained. When users are leaving the study team, this should be reported to the study data manager within one week time. The data manager will then subsequently withdraw the access rights of this user.

**Training and eCRF manual**
WP3 will create a study specific manual for the use of RO and will also train the PI or delegate in the use of RO. Further site specific users must be trained by the PI or delegate.

**External data**
External data (e.g. of sample test results) will be merged with the eCRF study data using SAS. Details and timelines will be recorded in a separate implementation plan.

**Discrepancy management**
Due to the validation rules which are built into the eCRF, data inconsistencies might be detected. These inconsistencies could result in the generation of automated queries. Besides these automatic generated queries, manual queries can also be generated during data review by data management, monitors and medical reviewers. Both automatic and manual generated queries should be resolved by the persons that are entering the data into the system. Data will only be ready for data analysis after all queries are resolved. Julius DM is responsible for reporting on the query management.

**(Risk Based) Monitoring**
After data has been entered into RO it might be checked by monitors. The monitoring process might be based on well-defined rules that are applied to all subjects (like monitoring of all first visits) or on a flexible rule based on sites and variables (Risk Based monitoring). RO supports Risk Based Monitoring: the amount of monitoring can be determined on site and item level.

Data that has been SDV-ed can be checked and unchecked in the eCRF. If inconsistencies are found, the monitor can create a manual query to get the data changed or to get a valid explanation. If data is changed the SDV flag is automatically unchecked by the system.

The study coordinator should provide a detailed list of all variables that are SDV required and send this list to DM.

**Coding**
Medical coding dictionaries (e.g. MEDDRA or WHODD) can be used to categorise medical data (e.g. Adverse Events or medication). It is not anticipated for this study that DM will perform medical coding.

**Reports**
During the conduct of the clinical studies, DM will have a central role in providing information related to study progress, data quality and data safety of the clinical studies. RO has three real time online reports available which will give an actual overview of the status of study progress at the time of report creation:

- Inclusion status: number of included patient per site/overall
- Filled forms: status of forms per patient/site/overall
- Query status: number of queries per patient/site/overall
In close cooperation with the study team it is possible to create additional reports (e.g. related to data quality, data safety and support of data monitoring activities) either offline or online via a study specific study dashboard. Implementation of study specific reports requires specific timelines depending on the requirements. Details will be described in the study specific implementation plan.

**Database lock and sign off**
At the end of the study all data must be locked. It is not possible to add, delete or change data that is in locked state. Once all data has been locked for a subject the Local Investigator can sign off the subject’s data. After sign off all RO access rights will be revoked for data entry.

In the rare case that an update after lock is necessary, the Project manager must approve the unlocking of the database. After approval the data manager will provide access rights again to the site to update the data. After update the database is locked again and requires re-signing of the patient’s data.

Because locking the database requires a lot of time, it is very important to start with the data cleaning process as soon as possible. Once data entry is started a detailed locking plan including checklist should be created by DM.

**Quality management system**
DM works with their own quality management system. Several Standard operating procedures (SOP) and Work instructions (WI) are used:

- Procedure Authorisation LAN
- Project Implementation RO
- Procedure Testing
- Procedure Data Locking/unlocking
- Procedure Data delivery
- Procedure Project closing
- Testing new study and project change request
- Configuration project
- Designing forms database and rules
- Export research data
- Research Online usage instructions
- Database downtime
- Directory structure

**Sample data**
The Central Lab in Antwerp uses the SLIMS system to register collected samples during the ARI2.0 trial and the enhanced PPAS. This means that the SLIMS system will be the biobank database within these studies. Registration of the collected samples, however, will be done initially in the eCRF within Research Online by the local labs. Entered data in RO will subsequently automatically be send to the RO DWH and subsequently the sample collection data to the RECOVER-CDR. An automatic connection between the RECOVER-CDR and the SLIMS system will be in place in order to send data of the collected samples from RECOVER-CDR to SLIMS. Based on the information in SLIMS a shipment manifest will be produced by the Central Lab in order for the Local Labs to ship the collected samples to the Central Lab.

The Central Lab and partners will analyse collected samples. Analyse test results will be entered in SLIMS and the integration between SLIMS and the RECOVER-CDR will send sample analyses results entered in SLIMS to the RECOVER-CDR.
DM will take care of processing sample analyses results within the RECOVER-CDR and merges these with clinical data from the eCRF and enhanced PPAS to analyse datasets.

Reconciliation processes will be set up to check consistencies of samples collected according to the local labs and samples received in the Central Lab and between sample analyses results entered in SLIMS and present in the RECOVER-CDR. Details of these processes are not known yet but will be described in more detail in subsequent DMP’s.

**RECOVER Central data repository**
The data warehouse will be populated with collected data from the RECOVER project. This data warehouse will be the RECOVER Central Data Repository (RECOVER-CDR) and will comprise of the following data:
- Enhanced PPAS eSurvey data and MERMAID ARI 1.0 and ARI 2.0 eCRF data collected using Research Online. The direct web service connection between Research Online and the RO DWH will take care of nearly real time data availability.
- Sample test analyses results data. Connections between SLIMS and DWH will be realized to take care that sample data will be available within the DWH.
- Currently it is not known if data coming from CASTOR EDC (WP3), data from the dedicated diary Apps from WP6 and data from WP5 will also be stored into the RECOVER-CDR. In subsequent DMP’s this will be described in more detail.

**Information provision and data access**
All data residing in the RECOVER-CDR will be directly accessible by the BI tool ‘Power BI’ for reporting and visualization purposes. In cooperation with stakeholders dashboards will be created with information to facilitate study management (e.g. study progress and data quality related reports and visualizations).

**Data privacy**

**General principals within RECOVER**
The EU General Data Protection Regulation (GDPR) 2018, includes special rules on the collection and use of personal data for medical research and public health purposes. Emerging legislation will be monitored to ensure the long-term and on-going legitimacy of approaches to data privacy. All data processing within and beyond the project will be done in compliance with the EU GDPR. The following general principles will apply to all research conducted in RECOVER.

Data handling will comply with current national and EU legislation, including:
- Personally identifiable information is adequately protected;
- All (pseudonimised) personal data of study subjects, is regarded as confidential information.
- Anonymisation/de-identification is conducted appropriately;
- Ethical review is completed as required.

Each study member will be responsible for the confidentiality and security of personal identifiable information and for complying with their own SOPs and any shared study specific SOPs.

In general terms, appropriate data protection principles will be observed, including:
- Data are fairly and lawfully processed;
- The amount of data collected is relevant and not excessive;
- All reasonable efforts are taken to ensure data accuracy;
- The data are used in accordance with the rights of the study participant;
- The data are stored securely;

Key references that govern the use of human data are listed below. This list is not intended to be all inclusive.
- Convention for the Protection of Individuals with Regard to Automatic Processing of Personal Data (1985)
- Recommendation No. R (97) 5 on the Protection of Medical Data (1997)
• Declaration on Ethical Considerations Regarding Health Databases (2002)
• Data protection and privacy ethical guidelines of the Experts Working Group on data protection and privacy (2009)
• Article 29 Data Protection Working Party, Vademecum on Notification Requirements (2006)
• EU General Data Protection Regulation (GDPR) 2018

Specific measurements to protect personal data
The staff of the various studies that will be conducted within RECOVER will ensure that the participants’ anonymity is maintained. Only anonymised patient data will be captured on the CRF, sample tubes and any electronic database. Unique study identifiers (Subject ID) will be used to identify the subjects in the eCRF database. Local teams will log patient identifiable data (like name, contact data and date of birth) in a separate data source to link the subject to the correct Subject ID number. These data sources, that are only accessible for the local authorised trial staff, are stored at a secured location on site. This prevents that a direct link can be established between personally identifiable data and clinical research data in the central database. After collection of the data and verification/data querying has been completed the link will be destroyed at the local study sites, to ensure there cannot be any link to participants, rendering the data anonymous at this point.

Anonymised clinical trial data will be captured using Research Online. This data management system meets all GCP guidelines for electronic data collection in terms of protecting data integrity and securing the information collected. More information is listed in chapter 6a.

RECOVER Data

In the following table a listing is provided of all types of data that will be generated by the various WP’s:

<table>
<thead>
<tr>
<th>WP2</th>
<th>Enhanced PPAS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>From each included patient the following baseline data will be gathered: demographics, respiratory tract infection symptoms and severity, comorbidity, measurements, tests, treatment, provided advices.</td>
</tr>
<tr>
<td></td>
<td>From each patient, a combined throat and nasal swab will be taken, which will be used to determine the cause of infection, thereby yielding microbiological data.</td>
</tr>
<tr>
<td></td>
<td>Finally, follow-up data will be collected at two time points, 1 and 4 weeks: the course of disease, return to usual daily activity, medication used, preventive measures taken, respiratory disease in family members, complications like pneumonia, and hospitalisation -days in hospital, medication, ventilation- and death.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WP3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>For ARI 1.0, the protocol for the MERMAIDS-ARI study will be re-implemented, a prospective, non-randomised observational study of CA-ARI in selected European countries. MERMAIDS-ARI enrolled patients presenting to primary care or being hospitalized with an acute respiratory illness. The protocol will be minimally amended to capture additional aspects relevant to SARS-CoV-2 infections, to avoid full IRB revision and newcontracts (which would delay start of enrollment). Reactivation includes both the 29 hospitals and the 9 primary care settings.</td>
</tr>
<tr>
<td></td>
<td>For ARI 2.0, the existing MERMAIDS-ARI protocol will be adapted to capture additional aspects relevant to SARS-CoV-2 infections, collect more and targeted biological sampling of confirmed SARS-CoV-2 infections needed for WP5 and WP6, and to enroll children (non-eligible in part I). The unified aim of both study parts is to establish the prevalence, disease spectrum and severity, clinical features, management, risk factors, spread and outcomes of SARS-CoV-2 infection in hospital care in European countries. For this purpose, we will align as much as possible with the ISARIC-CCP protocol, with stratified recruitment in tiers of</td>
</tr>
</tbody>
</table>
the protocol for sub-cohorts of patients.

- **Rapid survey of health care professionals**: We will rapidly survey staff (doctors, nurses, administrators etc.) working in ER and ICU settings across our hospital networks to assess perceptions of risk, knowledge and views of recommended IPC procedures.

### WP4

- Exhaustive etiologic diagnosis will be performed on the samples collected from patients included in the SARS-CoV-2 clinical trials, using state-of-the-art PCR technology developed and/or validated through WP4 and through other EU-funded projects such as GRACE, PREPARE, EVD-LabNet (www.evd-labnet.eu) and EVAg (www.european-virus-archive.com). For longitudinally sampled patients, PCR based etiologic diagnosis will be complemented with the suite of assays developed in WP5 for antibody profiling, transcriptome analysis, virus sequencing e.a.

### WP5

- In the PREPARE project, host transcriptomes were analysed of patients infected with a range of common respiratory pathogens, presenting in primary care or admitted to hospitals. Using these standardized analysis pipelines developed in PREPARE, genome-wide expression profiling will be done by microarray- and RNA seq-based methods in peripheral blood and nasopharyngeal specimens from patients with mild (primary care) and moderate to severe (hospitalized) SARS-CoV-2 infections, collected in observational studies of WP3. Gene expression profiles from SARS-CoV-2 infected patients will be analysed in the context of those from patients with other laboratory-confirmed acute respiratory infections, including human CoV infections (n=75), generated in the PREPARE MERMAIDS-ARI study. We will compare the transcriptome of patients with mild and severe SARS-CoV-2 infection, and analyse them comparatively for possible signatures associated with severity. In addition, the antibody landscapes for the patient groups included in this analysis will be compared.

- Using samples from patients, virus strains will be amplified by cell culture isolation. Genome will be sequenced. We will do characterization using growth curve and we will implement some relevant assays developed and validated by EU partners.

### WP6

- Studies will be conducted within households and health care workers to investigate transmission of the virus responsible for COVID-19 disease. Dedicated apps will be used to collect daily data. Samples (swabs) will be taken and analysed.

- Data will be collected on knowledge, perceptions, fears, attitudes and behaviors with respect to the SARS-CoV-2 epidemic. This will be done in France through the participative platform GrippeNet.fr, developed by Inserm and Sante publique France since 2011 to monitor influenza-like-illness and associated behaviors.

WP1 will not collect any research data. At this stage details are not known about data generation, processing or archiving of WP5 and WP6 and therefore the procedures described in this DMP will only apply to data within WP2, WP3 and WP4.

**Data stewardship**

Data stewardship involves all activities required to ensure that collected research data are findable, accessible, interoperable, and reusable (FAIR) in the long term. This includes data management, archiving, and reuse by third parties.

**Data standards and metadata**

The enhanced PPAS survey data of WP2 will be collected using an eCRF within Research Online. Also the REMAP-CAP and MERMAID ARI 1.0 studies are already present in Research Online. During the initial set up of the data formats they do not match a predefined standard. Data will be stored in a central database and can be exported and processed for usage in any desirable format and standard. Further requirements for data formats and standards will be defined.
during the conduct of the project and will be described in subsequent versions of the DMP.

The ARI 2.0 CRF of WP3 will as much as possible match the international ISARIC-WHO which is used to collect data on suspected or confirmed cases of COVID-19. This CRF is also used within the Clinical Characterization Protocol. The datadictionary of the ISARIC-WHO CRF will be used to map data collected in ARI 1.0 and ARI 2.0 as much as possible to the ISARIC-WHO data. This will be done in order to be able to pool data with data collected within other studies.

**Data curation and preservation**

Curation of collected data will be defined in detail during the conduct of the project and will be described in subsequent versions of the DMP. In principle data captured related to the enhanced PPAS survey data and data captured for the ARI studies will be curated by the data management department of the Julius Center (UMCU). Meta data will be added to the data by means of variable and value labels. Processed data for specific analyses will be curated by the applicable WP. After data has been curated it will be integrated into a central repository (RECOVER-CDR) for preservation and future analysis.

**Making data reusable**

Collected data within RECOVER will be managed and integrated into a central repository (RECOVER-CDR) as much as possible. This data includes at least clinical and sample data collected for the enhanced PPAS of WP2 and all studies conducted within WP3. An online secure data portal for data sharing of this central repository (RECOVER-CDR) will be developed and made accessible for all RECOVER investigators to query, analyse and download final curated datasets.

**Data sharing**

Data residing in the RECOVER-CDR can be made available to third parties. Details for the various collected datasets are currently unknown but in principle a managed data access and sharing procedure will be developed and agreements will be put in place to allow access to third parties that wish to use the RECOVER study data for secondary analysis after the closure of the study.

General principle will be that data will be as open as possible but as closed as needed. Therefore data will not be made completely openly accessible in line with national, European and international legal, ethical and privacy concerns and to ensure that data sharing complies with the GDPR. Any shared data will be minimized and anonymized as far as possible for the requested purpose (to comply with GDPR legislation).

Currently also the sharing of data using the GO-FAIR initiative (https://www.go-fair.org/) is under investigation. Recently this consortium has started the implementation network: Virus Outbreak Data Network (VODAN https://www.go-fair.org/implementation-networks/overview/vodan/) to enable sharing of data collected during the COVID-19 pandemic. This initiative might be used to share data of the ARI studies that are harmonized with the ISARIC-WHO CRF. This will be done by creating a ‘FAIR Data Point’ which will be machine readable accessible and might be used for AI approaches. More details of this initiative will be outlined in subsequent DMP’s.

**Data archiving**

At the end of the project, the collected study data will be under the guardianship of the UMC Utrecht and preserved in a secure manner – a continuation of the data storage during the project, meaning encrypted and on a password protected encrypted server. No personal identifiable data will be held (only pseudonymised study number). All data will be kept for a minimum preservation term of 15 years on the secured server of the UMCU, unless otherwise specified in the contracts with the original owners of the routine data in the different participating countries.

User privileges will also be set so that some users may be allowed to export data from the central repository but will have the data de-identification methods imposed as a means of preventing them from exporting sensitive data, either mistakenly or intentionally.
### ESTIMATED BUDGET FOR THE ACTION

<table>
<thead>
<tr>
<th>Form of costs</th>
<th>Actual</th>
<th>Unit1</th>
<th>Unit2</th>
<th>Actual</th>
<th>Actual</th>
<th>Actual</th>
<th>Unit3</th>
<th>Flat-rate10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>b</td>
<td>c</td>
<td>d [1]</td>
<td>e [2]</td>
<td>f</td>
<td>g</td>
<td>i1</td>
</tr>
<tr>
<td><strong>A. Direct personnel costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>25%</td>
</tr>
<tr>
<td>A.1 Employees (or equivalent)</td>
<td>234 883.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>405 000.00</td>
<td>0.00</td>
<td>150 971.25</td>
</tr>
<tr>
<td>A.2 Natural persons under direct contract</td>
<td>47 615.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>11 903.75</td>
<td>0.00</td>
<td>59 518.75</td>
</tr>
<tr>
<td>A.3 Seconded persons</td>
<td>1 074 000.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>171 875.00</td>
<td>0.00</td>
<td>859 175.00</td>
</tr>
<tr>
<td><strong>B. Direct costs of subcontracting</strong></td>
<td>143 000.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>241 000.00</td>
<td>0.00</td>
<td>80 750.00</td>
</tr>
<tr>
<td><strong>C. Direct costs of financial support</strong></td>
<td>528 905.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>92 098.00</td>
<td>0.00</td>
<td>80 150.75</td>
</tr>
<tr>
<td><strong>D. Other direct costs</strong></td>
<td>210 000.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>70 000.00</td>
<td>0.00</td>
<td>70 000.00</td>
</tr>
<tr>
<td><strong>E. Indirect costs</strong></td>
<td>205 400.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>155 000.00</td>
<td>0.00</td>
<td>80 600.00</td>
</tr>
<tr>
<td><strong>F. Special unit costs</strong></td>
<td>99 154.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>129 440.00</td>
<td>0.00</td>
<td>286 000.00</td>
</tr>
<tr>
<td><strong>G. Direct costs of (fin. support) infrastructure</strong></td>
<td>25 000.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>4 000.00</td>
<td>0.00</td>
<td>7 250.00</td>
</tr>
<tr>
<td><strong>H. IPS</strong></td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Total consortium</strong></td>
<td>2 819 112.00</td>
<td>0.00</td>
<td>0.00</td>
<td>1 361 144.00</td>
<td>0.00</td>
<td>705 564.00</td>
<td>0.00</td>
<td>4 995 820.00</td>
</tr>
</tbody>
</table>

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1. See Article 6 for the eligibility conditions.
2. Indirect costs already covered by an operating grant (received under any EU or Euratom funding programme; see Article 6.5(b)) are ineligible under the GA. Therefore, a beneficiary/linking third party that receives an operating grant during the action's duration cannot declare indirect costs for the year(s) reporting period(s) covered by the operating grant, unless it can demonstrate that the operating grant does not cover any costs of the action (see Article 6.2.E).
3. This is the theoretical amount of EU contribution that the system calculates automatically (by multiplying all the budgeted costs by the reimbursement rate). This theoretical amount is capped by the 'maximum grant amount' (that the Commission decided to grant for the action) (see Article 5.1).
4. The 'maximum grant amount' is the maximum grant amount decided by the Commission. It normally corresponds to the requested grant, but may be lower.
5. Depending on its type, this specific cost category will or will not cover indirect costs. Specific unit costs that include indirect costs are: costs for energy efficiency measures in buildings, access costs for providing trans-national access to research infrastructure and costs for clinical studies.
6. See Article 5 for the forms of costs.
7. See Annex 2a 'Additional information on the estimated budget' for the details (costs per hour (hourly rate)).
8. See Annex 1a 'Information for indirect costs' for the details (units, costs per unit).
9. See Annex 2b 'Additional information on the estimated budget' for the details (units, costs per unit).
10. See Annex 2a 'Addtional information on the estimated budget' for the details (units, costs per unit).

**Flat rate:** 25% of eligible direct costs, from which are excluded: direct costs of subcontracting, costs of in-kind contributions not used on premises, direct costs of financial support, and unit costs declared under budget category F if they include indirect costs (see Article 6.2.E).

---

**See Annex 2a 'Additional information on the estimated budget' for the details (units, costs per unit).**

**Only specific unit costs that do not include indirect costs.**

**See Article 5 for beneficiaries not receiving funding.**

**Only for linked third parties that receive funding.**
ANNE 2a

ADDITIONAL INFORMATION ON THE ESTIMATED BUDGET

- Instructions and footnotes in blue will not appear in the text generated by the IT system (since they are internal instructions only).
- For options [in square brackets]: the applicable option will be chosen by the IT system. Options not chosen will automatically not appear.
- For fields in [grey in square brackets] (even if they are part of an option as specified in the previous item): IT system will enter the appropriate data.

⚠️ Transitory period: Until SyGMA fully supports Annex 2a, you must prepare it manually (using this template by choosing and deleting the options/entering the appropriate data). For the ‘unit cost tables’: either fill them out manually or use currently existing tables from Annex 1 or the proposal. The document can then be uploaded in SyGMA and attached to the grant agreement.

Unit cost for SME owners/natural beneficiaries without salary

1. Costs for a /SME owner//beneficiary that is a natural person/ not receiving a salary

Units: hours worked on the action

Amount per unit (‘hourly rate’): calculated according to the following formula:

\[
\text{Amount per unit} = \frac{\text{the monthly living allowance for researchers in MSCA-IF actions} / 143 \, \text{hours}}{\text{country-specific correction coefficient of the country where the beneficiary is established}}
\]

The monthly living allowance and the country-specific correction coefficients are set out in the Work Programme (section 3 MSCA) in force at the time of the call:

- for calls before Work Programme 2018-2020:
  - for the monthly living allowance: **EUR 4 650**

- for calls under Work Programme 2018-2020:
  - for the monthly living allowance: **EUR 4 880**
  - for the country-specific correction coefficients: see Work Programme 2018-2020 (available on the Participant Portal Reference Documents page)

[additional OPTION for beneficiaries/linked third parties that have opted to use the unit cost (in the proposal/with an amendment):] For the following beneficiaries/linked third parties, the amounts per unit (hourly rate) are fixed as follows:

- beneficiary/linked third party [short name]: EUR [insert amount]
- beneficiary/linked third party [short name]: EUR [insert amount]

[same for other beneficiaries/linked third parties, if necessary]

Estimated number of units: see Annex 2
Energy efficiency measures unit cost

2. Costs for energy efficiency measures in buildings

Unit: m² of eligible ‘conditioned’ (i.e. built or refurbished) floor area

Amount per unit*: see (for each beneficiary/link third party and BEST table) the ‘unit cost table’ attached

* Amount calculated as follows:
{EUR 0.1 \times \text{estimated total kWh saved per m}^2 \text{ per year} \times 10} 

Estimated number of units: see (for each beneficiary/link third party and BEST table) the ‘unit cost table’ attached

Unit cost table (energy efficiency measures unit cost)¹

<table>
<thead>
<tr>
<th>Short name beneficiary/link third party</th>
<th>BEST No</th>
<th>Amount per unit</th>
<th>Estimated No of units</th>
<th>Total unit cost (cost per unit x estimated no of units)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

¹ Data from the ‘building energy specification table (BEST)’ that is part of the proposal and Annex 1.
Research infrastructure unit cost

3. Access costs for providing trans-national access to research infrastructure

Units: see (for each access provider and installation) the ‘unit cost table’ attached

Amount per unit*: see (for each access provider and installation) the ‘unit cost table’ attached

* Amount calculated as follows:
average annual total access cost to the installation (over past two years*)
average annual total quantity of access to the installation (over past two years*)

Estimated number of units: see (for each access provider and installation) the ‘unit cost table’ attached

Unit cost table (access to research infrastructure unit cost)\(^5\)

<table>
<thead>
<tr>
<th>Short name access provider</th>
<th>Short name infrastructure</th>
<th>Installation</th>
<th>Unit of access</th>
<th>Amount per unit</th>
<th>Estimated No of units</th>
<th>Total unit cost (cost per unit x estimated no of units)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>Short name</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Clinical studies unit cost

4. Costs for clinical studies

Units: patients/subjects that participate in the clinical study

Amount per unit*: see (for each sequence (if any), clinical study and beneficiary/linked third party) the ‘unit cost table’ attached

* Amount calculated, for the cost components of each task, as follows:

For personnel costs:

- For personnel costs of doctors: ‘average hourly cost for doctors’, i.e.:
  \[
  \text{certified or auditable total personnel costs for doctors for year N-1} \\
  \times \frac{1720 \times \text{number of full-time-equivalent for doctors for year N-1}}{\text{estimated number of hours to be worked by doctors for the task (per participant)}}
  \]

- For personnel costs of other medical personnel: ‘average hourly cost for other medical personnel’, i.e.:
  \[
  \text{certified or auditable total personnel costs for other medical personnel for year N-1} \\
  \times \frac{1720 \times \text{number of full-time-equivalent for other medical personnel for year N-1}}{\text{estimated number of hours to be worked by other medical personnel for the task (per participant)}}
  \]

---

2 Unit of access (e.g. beam hours, weeks of access, sample analysis) fixed by the access provider in proposal.
3 In exceptional and duly justified cases, the Commission/Agency may agree to a different reference period.
4 In exceptional and duly justified cases, the Commission/Agency may agree to a different reference period.
5 Data from the ‘table on estimated costs/quantity of access to be provided’ that is part of the proposal and Annex 1.
For personnel costs of technical personnel: ‘average hourly cost for technical personnel’, i.e.:

\[
\text{\{certified or auditable total personnel costs for technical personnel for year N-1} \\
\times \text{\{1720 * number of full-time-equivalent for technical personnel for year N-1\}} \\
\times \text{estimated number of hours to be worked by technical personnel for the task (per participant)}
\]

‘total personnel costs’ means actual salaries + actual social security contributions + actual taxes and other costs included in the remuneration, provided they arise from national law or the employment contract/equivalent appointing act

For consumables:

For each cost item: ‘average price of the consumable’, i.e.:

\[
\text{\{certified or auditable total costs of purchase of the consumable in year N-1} \\
\times \text{\{total number of items purchased in year N-1\}} \\
\times \text{estimated number of items to be used for the task (per participant)}
\]

‘total costs of purchase of the consumable’ means total value of the supply contracts (including related duties, taxes and charges such as non-deductible VAT) concluded by the beneficiary for the consumable delivered in year N-1, provided the contracts were awarded according to the principle of best value- for-money and without any conflict of interests

For medical equipment:

For each cost item: ‘average cost of depreciation and directly related services per unit of use’, i.e.:

\[
\text{\{certified or auditable total depreciation costs in year N-1 + certified or auditable total costs of purchase of services in year N-1 for the category of equipment concerned\} } \\
\times \text{\{total capacity in year N-1\}} \\
\times \text{estimated number of units of use of the equipment for the task (per participant)}
\]

‘total depreciation costs’ means total depreciation allowances as recorded in the beneficiary’s accounts of year N-1 for the category of equipment concerned, provided the equipment was purchased according to the principle of best value for money and without any conflict of interests + total costs of renting or leasing contracts (including related duties, taxes and charges such as non-deductible VAT) in year N-1 for the category of equipment concerned, provided they do not exceed the depreciation costs of similar equipment and do not include finance fees

For services:

For each cost item: ‘average cost of the service per study participant’, i.e.:

\[
\text{\{certified or auditable total costs of purchase of the service in year N-1} \\
\times \text{\{total number of patients or subjects included in the clinical studies for which the service was delivered in year N-1\}}
\]

‘total costs of purchase of the service’ means total value of the contracts concluded by the beneficiary (including related duties, taxes and charges such as non-deductible VAT) for the specific service delivered in year N-1 for the conduct of clinical studies, provided the contracts were awarded according to the principle of best value for money and without any conflict of interests

For indirect costs:

\[
\text{\{\{cost component ‘personnel costs’ + cost component ‘consumables’ + cost component ‘medical equipment’\} } \\
\times \text{\{costs of in-kind contributions provided by third parties which are not used on the beneficiary’s premises + costs of providing financial support to third parties (if any)\}} \\
\times \text{25%}
\]
The estimation of the resources to be used must be done on the basis of the study protocol and must be the same for all beneficiaries/linked third parties/third parties involved.

The year N-1 to be used is the last closed financial year at the time of submission of the grant application.

Estimated number of units: see (for each clinical study and beneficiary/linked third party) the ‘unit cost table’ attached

Unit cost table: clinical studies unit cost

<table>
<thead>
<tr>
<th>Task, Direct cost categories</th>
<th>Resource per patient</th>
<th>Costs year N-1 Beneficiary 1 [short name]</th>
<th>Costs year N-1 Beneficiary 2a [short name]</th>
<th>Costs year N-1 Linked third party 1a [short name]</th>
<th>Costs year N-1 Linked third party 2a [short name]</th>
<th>Costs year N-1 Third party giving in-kind contributions 1 [short name]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Task No. 1 Blood sample</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Personnel costs:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Doctors</td>
<td>n/a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Other Medical Personnel</td>
<td>Phlebotomy (nurse), 10 minutes</td>
<td>8,33 EUR</td>
<td>11,59 EUR</td>
<td>10,30 EUR</td>
<td>11,00 EUR</td>
<td>9,49 EUR</td>
</tr>
<tr>
<td>- Technical Personnel</td>
<td>Sample Processing (lab technician), 15 minutes</td>
<td>9,51 EUR</td>
<td>15,68 EUR</td>
<td>14,60 EUR</td>
<td>15,23 EUR</td>
<td>10,78 EUR</td>
</tr>
<tr>
<td>(b) Costs of consumables:</td>
<td>Syringe</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
</tr>
<tr>
<td></td>
<td>Cannula</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
</tr>
<tr>
<td></td>
<td>Blood container</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
</tr>
<tr>
<td>(c) Costs of medical equipment:</td>
<td>Use of -80° deep freezer, 60 days</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
</tr>
<tr>
<td></td>
<td>Use of centrifuge, 15 minutes</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
</tr>
<tr>
<td>(d) Costs of services</td>
<td>Cleaning of XXX</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
</tr>
<tr>
<td>(e) Indirect costs (25% flat-rate)</td>
<td></td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
<td>XX EUR</td>
</tr>
</tbody>
</table>

Task No. 2

...=

Amount per unit (unit cost sequence 1): XX EUR XX EUR XX EUR XX EUR XX EUR

Sequence No. 2

Task No. 1

---

Same table as in proposal and Annex 1.
<table>
<thead>
<tr>
<th>XXX</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Personnel costs:</td>
</tr>
<tr>
<td>- Doctors</td>
</tr>
<tr>
<td>- Other Medical Personnel</td>
</tr>
<tr>
<td>- Technical Personnel</td>
</tr>
<tr>
<td>(b) Costs of consumables:</td>
</tr>
<tr>
<td>XXX</td>
</tr>
<tr>
<td>XXX</td>
</tr>
<tr>
<td>(c) Costs of medical equipment:</td>
</tr>
<tr>
<td>XXX</td>
</tr>
<tr>
<td>XXX</td>
</tr>
<tr>
<td>(d) Costs of services</td>
</tr>
<tr>
<td>XXX</td>
</tr>
<tr>
<td>(e) Indirect costs (25% flat-rate)</td>
</tr>
<tr>
<td>XX EUR</td>
</tr>
</tbody>
</table>

Task No. 2

... 

Amount per unit (unit cost sequence 2): XX EUR XX EUR XX EUR XX EUR XX EUR 

... 

Amount per unit (unit cost entire study): XX EUR XX EUR XX EUR XX EUR XX EUR
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUT PASTEUR (IP), established in RUE DU DOCTEUR ROUX 25-28, PARIS CEDEX 15 75724, France, VAT number: FR65775684897, (‘the beneficiary’), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No (‘2’)
in Grant Agreement No 101003589 (‘the Agreement’)
between UNIVERSITEIT ANTWERPEN and the European Union (‘the EU’), represented by the European Commission (‘the Commission’),

for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response (RECoVER)’.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITAIR MEDISCH CENTRUM UTRECHT (UMC UTRECHT), established in HEIDELBERGLAAN 100, UTRECHT 3584 CX, Netherlands, VAT number: NL004205315B01, (‘the beneficiary’), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No (‘3’)
in Grant Agreement No 101003589 (‘the Agreement’)
between UNIVERSITEIT ANTWERPEN and the European Union (‘the EU’), represented by the European Commission (‘the Commission’),

for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response (RECoVER)’.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM (ERASMUS MC),
established in DR MOLEWATERPLEIN 40, ROTTERDAM 3015 GD, Netherlands, VAT number:
NL801427228B01, (‘the beneficiary’), represented for the purpose of signing this Accession Form
by the undersigned,

hereby agrees

to become beneficiary No (‘4’)
in Grant Agreement No 101003589 (‘the Agreement’)

between UNIVERSITEIT ANTWERPEN and the European Union (‘the EU’), represented by the
European Commission (’the Commission’),

for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response (RECoVER)’.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement,
in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in
accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD (UOXF), established in WELLINGTON SQUARE UNIVERSITY OFFICES, OXFORD OX1 2JD, United Kingdom, VAT number: GB125506730, (‘the beneficiary’), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No (‘5’)
in Grant Agreement No 101003589 (‘the Agreement’)

between UNIVERSITEIT ANTWERPEN and the European Union (‘the EU’), represented by the European Commission (‘the Commission’),

for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response (RECoVER)’.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CHARITE - UNIVERSITAETSMEDECIN BERLIN (CHARITE), established in Chariteplatz 1, BERLIN 10117, Germany, VAT number: DE228847810, (‘the beneficiary’), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No (‘6’)
in Grant Agreement No 101003589 (‘the Agreement’)
between UNIVERSITEIT ANTWERPEN and the European Union (‘the EU’), represented by the European Commission (‘the Commission’),

for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response (RECoVER)’.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM),
established in RUE DE TOLBIAC 101, PARIS 75654, France, VAT number: FR31180036048, (‘the beneficiary’), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No (‘7’) in Grant Agreement No 101003589 (‘the Agreement’)

between UNIVERSITEIT ANTWERPEN and the European Union (‘the EU’), represented by the European Commission (‘the Commission’),

for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response (RECoVER)’.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ACADEMISCH MEDISCH CENTRUM BIJ DE UNIVERSITEIT VAN AMSTERDAM (AMC), established in MEIBERGDREEF 15, AMSTERDAM 1105AZ, Netherlands, VAT number: NL004627672B01, (‘the beneficiary’), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No (‘8’)
in Grant Agreement No 101003589 (‘the Agreement’)
between UNIVERSITEIT ANTWERPEN and the European Union (‘the EU’), represented by the European Commission (‘the Commission’),

for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response (RECoVER)’.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDAZIONE PENTA - FOR THE TREATMENT AND CARE OF CHILDREN WITH HIV AND RELATED DISEASES - ONLUS (PENTA), established in CORSO STATI UNITI 4, PADOVA 35127, Italy, VAT number: IT04150680280, (‘the beneficiary’), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No (‘9’)
in Grant Agreement No 101003589 (‘the Agreement’)

between UNIVERSITEIT ANTWERPEN and the European Union (‘the EU’), represented by the European Commission (‘the Commission’),

for the action entitled ‘Rapid European SARS-CoV-2 Emergency research Response (RECoVER)’.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUT PASTEUR OF SHANGHAI, CHINESE ACADEMY OF SCIENCES (IPS), established in SOUTH CHONGQING ROAD BUILDING 2 LUWAN DISTRICT 225, SHANGHAI 200025, China (People's Republic of), ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('10')
in Grant Agreement No 101003589 ('the Agreement')
between UNIVERSITEIT ANTWERPEN and the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'Rapid European SARS-CoV-2 Emergency research Response (RECoVER)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any amendments to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and conditions it sets out.

SIGNATURE

For the beneficiary
The beneficiary/linked third party hereby confirms that:

The information provided is complete, reliable and true.

The costs declared are eligible (see Article 6).

The costs can be substantiated by adequate records and supporting documentation that will be produced upon request or in the context of checks, reviews, audits and investigations (see Articles 17, 18 and 22).

For the last reporting period that all the receipts have been declared (see Article 5.3.3).

1 Please declare all eligible costs, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Only amounts that were declared in your individual financial statements can be taken into account later on, in order to replace other costs that are found to be ineligible.

2 See Article 6 for the eligibility conditions

3 The indirect costs claimed must be free of any amounts covered by an operating grant [received under any EU or Euratom funding programme; see Article 6.2.E]. If you have received an operating grant during this reporting period, you cannot claim indirect costs unless you can demonstrate that the operating grant does not cover any costs of the action.

4 See Article 6 for the forms of costs

5 Flat rate: 25% of eligible direct costs, from which are excluded: direct costs of subcontracting, costs of in-kind contributions not used on premises, direct costs of financial support, and unit costs declared under budget category F if they include indirect costs (see Article 6.2.E)

6 Only specific unit costs that do not include indirect costs

### MODEL ANNEX 4 FOR H2020 GENERAL MGA — MULTI

**FINANCIAL STATEMENT FOR [BENEFICIARY [name]]/[LINKED THIRD PARTY [name]] FOR REPORTING PERIOD [reporting period]**

<table>
<thead>
<tr>
<th>Form of costs</th>
<th>A. Direct personnel costs</th>
<th>B. Direct costs of subcontracting</th>
<th>C. Direct costs of fin. support</th>
<th>D. Other direct costs</th>
<th>E. Indirect costs</th>
<th>F. Costs of ...</th>
<th>Total costs</th>
<th>Receipts</th>
<th>EU contribution</th>
<th>Reimbursement rate %</th>
<th>Maximum EU contribution</th>
<th>Requested EU contribution</th>
<th>Additional information</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A.1 Employees (or equivalent)</td>
<td>A.4 SME owners without salary</td>
<td>C.1 Financial support</td>
<td>D.1 Travel</td>
<td>E. Consulting</td>
<td>F.1 Costs of ...</td>
<td>g</td>
<td>h+i</td>
<td>i</td>
<td>j1</td>
<td>Total b</td>
<td>Total c</td>
<td>d</td>
</tr>
<tr>
<td></td>
<td>A.2 Natural persons under direct contract</td>
<td>A.5 Beneficiaries that are natural persons without salary</td>
<td>C.2 Prices</td>
<td>D.2 Equipment</td>
<td>E.1 Indirect costs</td>
<td>F.2 Costs of ...</td>
<td>g</td>
<td>h+i</td>
<td>i</td>
<td>j1</td>
<td>Total b</td>
<td>Total c</td>
<td>d</td>
</tr>
<tr>
<td></td>
<td>A.3 Seconded persons</td>
<td>A.6 Personnel for providing access to research infrastructure</td>
<td>C.3 Other goods and services</td>
<td>D.3 Other goods and services</td>
<td>E.2 Indirect costs</td>
<td>F.3 Costs of ...</td>
<td>g</td>
<td>h+i</td>
<td>i</td>
<td>j1</td>
<td>Total b</td>
<td>Total c</td>
<td>d</td>
</tr>
<tr>
<td></td>
<td>A.4 Employees under direct contract</td>
<td>A.5 Beneficiaries that are natural persons without salary</td>
<td>C.4 Costs of large research infrastructure</td>
<td>D.4 Costs of large research infrastructure</td>
<td>E.3 Indirect costs</td>
<td>F.4 Costs of ...</td>
<td>g</td>
<td>h+i</td>
<td>i</td>
<td>j1</td>
<td>Total b</td>
<td>Total c</td>
<td>d</td>
</tr>
<tr>
<td></td>
<td>A.6 Personnel for providing access to research infrastructure</td>
<td>A.7 Beneficiaries that are natural persons without salary</td>
<td>C.5 Costs of internally invoiced goods and services</td>
<td>D.5 Costs of internally invoiced goods and services</td>
<td>E.4 Indirect costs</td>
<td>F.5 Costs of ...</td>
<td>g</td>
<td>h+i</td>
<td>i</td>
<td>j1</td>
<td>Total b</td>
<td>Total c</td>
<td>d</td>
</tr>
</tbody>
</table>

The beneficiary/linked third party hereby confirms that:

The information provided is complete, reliable and true.

The costs declared are eligible (see Article 6).

The costs can be substantiated by adequate records and supporting documentation that will be produced upon request or in the context of checks, reviews, audits and investigations (see Articles 17, 18 and 22).

For the last reporting period that all the receipts have been declared (see Article 5.3.3).
ANNEX 5

MODEL FOR THE CERTIFICATE ON THE FINANCIAL STATEMENTS

- For options *italics in square brackets*: choose the applicable option. Options not chosen should be deleted.
- For fields in *grey in square brackets*: enter the appropriate data

TABLE OF CONTENTS

TERMS OF REFERENCE FOR AN INDEPENDENT REPORT OF FACTUAL FINDINGS ON COSTS DECLARED UNDER A GRANT AGREEMENT FINANCED UNDER THE HORIZON 2020 RESEARCH FRAMEWORK PROGRAMME

INDEPENDENT REPORT OF FACTUAL FINDINGS ON COSTS DECLARED UNDER A GRANT AGREEMENT FINANCED UNDER THE HORIZON 2020 RESEARCH FRAMEWORK PROGRAMME
Terms of Reference for an Independent Report of Factual Findings on costs declared under a Grant Agreement financed under the Horizon 2020 Research and Innovation Framework Programme

This document sets out the ‘Terms of Reference (ToR)’ under which

[OPTION 1: [insert name of the beneficiary] (‘the Beneficiary’)]  [OPTION 2: [insert name of the linked third party] (‘the Linked Third Party’), third party linked to the Beneficiary [insert name of the beneficiary] (‘the Beneficiary’)]

agrees to engage

[insert legal name of the auditor] (‘the Auditor’)

to produce an independent report of factual findings (‘the Report’) concerning the Financial Statement(s) drawn up by the [Beneficiary] [Linked Third Party] for the Horizon 2020 grant agreement [insert number of the grant agreement, title of the action, acronym and duration from/to] (‘the Agreement’), and
to issue a Certificate on the Financial Statements’ (‘CFS’) referred to in Article 20.4 of the Agreement based on the compulsory reporting template stipulated by the Commission.

The Agreement has been concluded under the Horizon 2020 Research and Innovation Framework Programme (H2020) between the Beneficiary and [OPTION 1: the European Union, represented by the European Commission (‘the Commission’)] [OPTION 2: the European Atomic Energy Community (Euratom,) represented by the European Commission (‘the Commission’)] [OPTION 3: the [Research Executive Agency (REA)] [European Research Council Executive Agency (ERCEA)] [Innovation and Networks Executive Agency (INEA)] [Executive Agency for Small and Medium-sized Enterprises (EASME)] (‘the Agency’), under the powers delegated by the European Commission (‘the Commission’).

The [Commission] [Agency] is mentioned as a signatory of the Agreement with the Beneficiary only. The [European Union][Euratom][Agency] is not a party to this engagement.

1.1 Subject of the engagement

The coordinator must submit to the [Commission][Agency] the final report within 60 days following the end of the last reporting period which should include, amongst other documents, a CFS for each beneficiary and for each linked third party that requests a total contribution of EUR 325 000 or more, as reimbursement of actual costs and unit costs calculated on the basis of its usual cost accounting practices (see Article 20.4 of the Agreement). The CFS must cover all reporting periods of the beneficiary or linked third party indicated above.

The Beneficiary must submit to the coordinator the CFS for itself and for its linked third party(ies), if the CFS must be included in the final report according to Article 20.4 of the Agreement.

The CFS is composed of two separate documents:

- The Terms of Reference (‘the ToR’) to be signed by the [Beneficiary] [Linked Third Party] and the Auditor;

---

1 By which costs under the Agreement are declared (see template ‘Model Financial Statements’ in Annex 4 to the Grant Agreement).
- The Auditor’s Independent Report of Factual Findings (‘the Report’) to be issued on the Auditor’s letterhead, dated, stamped and signed by the Auditor (or the competent public officer) which includes the agreed-upon procedures (‘the Procedures’) to be performed by the Auditor, and the standard factual findings (‘the Findings’) to be confirmed by the Auditor.

If the CFS must be included in the final report according to Article 20.4 of the Agreement, the request for payment of the balance relating to the Agreement cannot be made without the CFS. However, the payment for reimbursement of costs covered by the CFS does not preclude the Commission [Agency,] the European Anti-Fraud Office and the European Court of Auditors from carrying out checks, reviews, audits and investigations in accordance with Article 22 of the Agreement.

1.2 Responsibilities

The [Beneficiary] [Linked Third Party]:
- must draw up the Financial Statement(s) for the action financed by the Agreement in compliance with the obligations under the Agreement. The Financial Statement(s) must be drawn up according to the [Beneficiary’s] [Linked Third Party’s] accounting and bookkeeping system and the underlying accounts and records;
- must send the Financial Statement(s) to the Auditor;
- is responsible and liable for the accuracy of the Financial Statement(s);
- is responsible for the completeness and accuracy of the information provided to enable the Auditor to carry out the Procedures. It must provide the Auditor with a written representation letter supporting these statements. The written representation letter must state the period covered by the statements and must be dated;
- accepts that the Auditor cannot carry out the Procedures unless it is given full access to the [Beneficiary’s] [Linked Third Party’s] staff and accounting as well as any other relevant records and documentation.

The Auditor:
- [Option 2 if the Beneficiary or Linked Third Party has an independent Public Officer: is a competent and independent Public Officer for which the relevant national authorities have established the legal capacity to audit the Beneficiary].
- [Option 3 if the Beneficiary or Linked Third Party is an international organisation: is an [internal] [external] auditor in accordance with the internal financial regulations and procedures of the international organisation].

The Auditor:
- must be independent from the Beneficiary [and the Linked Third Party], in particular, it must not have been involved in preparing the [Beneficiary’s] [Linked Third Party’s] Financial Statement(s);
- must plan work so that the Procedures may be carried out and the Findings may be assessed;
- must adhere to the Procedures laid down and the compulsory report format;
- must carry out the engagement in accordance with this ToR;
- must document matters which are important to support the Report;
- must base its Report on the evidence gathered;
- must submit the Report to the [Beneficiary] [Linked Third Party].
The Commission sets out the Procedures to be carried out by the Auditor. The Auditor is not responsible for their suitability or pertinence. As this engagement is not an assurance engagement, the Auditor does not provide an audit opinion or a statement of assurance.

1.3 Applicable Standards

The Auditor must comply with these Terms of Reference and with:

- the International Standard on Related Services (‘ISRS’) 4400 *Engagements to perform Agreed-upon Procedures regarding Financial Information* as issued by the International Auditing and Assurance Standards Board (IAASB);
- the *Code of Ethics for Professional Accountants* issued by the International Ethics Standards Board for Accountants (IESBA). Although ISRS 4400 states that independence is not a requirement for engagements to carry out agreed-upon procedures, the [Commission]/[Agency] requires that the Auditor also complies with the Code’s independence requirements.

The Auditor’s Report must state that there is no conflict of interests in establishing this Report between the Auditor and the Beneficiary [and the Linked Third Party], and must specify - if the service is invoiced - the total fee paid to the Auditor for providing the Report.

1.4 Reporting

The Report must be written in the language of the Agreement (see Article 20.7).

Under Article 22 of the Agreement, the Commission[, the Agency], the European Anti-Fraud Office and the Court of Auditors have the right to audit any work that is carried out under the action and for which costs are declared from [the European Union] [Euratom] budget. This includes work related to this engagement. The Auditor must provide access to all working papers (e.g. recalculation of hourly rates, verification of the time declared for the action) related to this assignment if the Commission [, the Agency], the European Anti-Fraud Office or the European Court of Auditors requests them.

1.5 Timing

The Report must be provided by /dd Month yyyy/.

1.6 Other terms

[The [Beneficiary] [Linked Third Party] and the Auditor can use this section to agree other specific terms, such as the Auditor’s fees, liability, applicable law, etc. Those specific terms must not contradict the terms specified above.]

Signature of the Auditor

Signature of the [Beneficiary][Linked Third Party]

---

2 Supreme Audit Institutions applying INTOSAI-standards may carry out the Procedures according to the corresponding International Standards of Supreme Audit Institutions and code of ethics issued by INTOSAI instead of the International Standard on Related Services (‘ISRS’) 4400 and the Code of Ethics for Professional Accountants issued by the IAASB and the IESBA.
Independent Report of Factual Findings on costs declared under Horizon 2020 Research and Innovation Framework Programme

(To be printed on the Auditor’s letterhead)

To

[ name of contact person(s)], [Position]

[ [Beneficiary’s] [Linked Third Party’s] name ]

[ Address]

[ dd Month yyyy]

Dear [Name of contact person(s)],

As agreed under the terms of reference dated [dd Month yyyy] with

[OPTION 1: [insert name of the beneficiary] (‘the Beneficiary’)]  [OPTION 2: [insert name of the linked third party] (‘the Linked Third Party’), third party linked to the Beneficiary [insert name of the beneficiary] (‘the Beneficiary’)],

we

[name of the auditor] (‘the Auditor’),

established at

[full address/city/state/province/country],

represented by

[name and function of an authorised representative],

have carried out the procedures agreed with you regarding the costs declared in the Financial Statement(s) of the [Beneficiary] [Linked Third Party] concerning the grant agreement [insert grant agreement reference: number, title of the action and acronym] (‘the Agreement’),

with a total cost declared of

[total amount] EUR,

and a total of actual costs and unit costs calculated in accordance with the [Beneficiary’s] [Linked Third Party’s] usual cost accounting practices’ declared of

[sum of total actual costs and total direct personnel costs declared as unit costs calculated in accordance with the [Beneficiary’s] [Linked Third Party’s] usual cost accounting practices] EUR

and hereby provide our Independent Report of Factual Findings (‘the Report’) using the compulsory report format agreed with you.

The Report

Our engagement was carried out in accordance with the terms of reference (‘the ToR’) appended to this Report. The Report includes the agreed-upon procedures (‘the Procedures’) carried out and the standard factual findings (‘the Findings’) examined.

---

3 By which the Beneficiary declares costs under the Agreement (see template ‘Model Financial Statement’ in Annex 4 to the Agreement).
The Procedures were carried out solely to assist the [Commission] [Agency] in evaluating whether the [Beneficiary’s] [Linked Third Party’s] costs in the accompanying Financial Statement(s) were declared in accordance with the Agreement. The [Commission] [Agency] draws its own conclusions from the Report and any additional information it may require.

The scope of the Procedures was defined by the Commission. Therefore, the Auditor is not responsible for their suitability or pertinence. Since the Procedures carried out constitute neither an audit nor a review made in accordance with International Standards on Auditing or International Standards on Review Engagements, the Auditor does not give a statement of assurance on the Financial Statements.

Had the Auditor carried out additional procedures or an audit of the [Beneficiary’s] [Linked Third Party’s] Financial Statements in accordance with International Standards on Auditing or International Standards on Review Engagements, other matters might have come to its attention and would have been included in the Report.

**Not applicable Findings**

We examined the Financial Statement(s) stated above and considered the following Findings not applicable:

**Explanation (to be removed from the Report):**

If a Finding was not applicable, it must be marked as ‘N.A.’ (‘Not applicable’) in the corresponding row on the right-hand column of the table and means that the Finding did not have to be corroborated by the Auditor and the related Procedure(s) did not have to be carried out.

The reasons of the non-application of a certain Finding must be obvious i.e.

i) if no cost was declared under a certain category then the related Finding(s) and Procedure(s) are not applicable;

ii) if the condition set to apply certain Procedure(s) are not met the related Finding(s) and those Procedure(s) are not applicable. For instance, for ‘beneficiaries with accounts established in a currency other than euro’ the Procedure and Finding related to ‘beneficiaries with accounts established in euro’ are not applicable. Similarly, if no additional remuneration is paid, the related Finding(s) and Procedure(s) for additional remuneration are not applicable.

**List here all Findings considered not applicable for the present engagement and explain the reasons of the non-applicability.**

....

**Exceptions**

Apart from the exceptions listed below, the [Beneficiary] [Linked Third Party] provided the Auditor all the documentation and accounting information needed by the Auditor to carry out the requested Procedures and evaluate the Findings.

**Explanation (to be removed from the Report):**

- If the Auditor was not able to successfully complete a procedure requested, it must be marked as ‘E’ (‘Exception’) in the corresponding row on the right-hand column of the table. The reason such as the inability to reconcile key information or the unavailability of data that prevents the Auditor from carrying out the Procedure must be indicated below.

- If the Auditor cannot corroborate a standard finding after having carried out the corresponding procedure, it must also be marked as ‘E’ (‘Exception’) and, where possible, the reasons why the Finding was not fulfilled and its possible impact must be explained here below.

**List here any exceptions and add any information on the cause and possible consequences of each exception, if known. If the exception is quantifiable, include the corresponding amount.**

....
Example (to be removed from the Report):

1. The Beneficiary was unable to substantiate the Finding number 1 on ... because ....
2. Finding number 30 was not fulfilled because the methodology used by the Beneficiary to
calculate unit costs was different from the one approved by the Commission. The differences
were as follows: ...
3. After carrying out the agreed procedures to confirm the Finding number 31, the Auditor found a
difference of __________EUR. The difference can be explained by ...

Further Remarks

In addition to reporting on the results of the specific procedures carried out, the Auditor would like to
make the following general remarks:

Example (to be removed from the Report):

1. Regarding Finding number 8 the conditions for additional remuneration were considered as
fulfilled because ....
2. In order to be able to confirm the Finding number 15 we carried out the following additional
procedures: ....

Use of this Report

This Report may be used only for the purpose described in the above objective. It was prepared solely
for the confidential use of the [Beneficiary] [Linked Third Party] and the [Commission] [Agency], and
only to be submitted to the [Commission] [Agency] in connection with the requirements set out in
Article 20.4 of the Agreement. The Report may not be used by the [Beneficiary] [Linked Third Party]
or by the [Commission] [Agency] for any other purpose, nor may it be distributed to any other parties.
The [Commission] [Agency] may only disclose the Report to authorised parties, in particular to the
European Anti-Fraud Office (OLAF) and the European Court of Auditors.

This Report relates only to the Financial Statement(s) submitted to the [Commission] [Agency] by the
[Beneficiary] [Linked Third Party] for the Agreement. Therefore, it does not extend to any other of
the [Beneficiary’s] [Linked Third Party’s] Financial Statement(s).

There was no conflict of interest\(^4\) between the Auditor and the Beneficiary \(\text{and Linked Third Party}\)
in establishing this Report. The total fee paid to the Auditor for providing the Report was EUR \(_______\)
(including EUR \(_______\) of deductible VAT).

We look forward to discussing our Report with you and would be pleased to provide any further
information or assistance.

[legal name of the Auditor]
[name and function of an authorised representative]
[dd Month yyyy]
Signature of the Auditor

\(^4\) A conflict of interest arises when the Auditor’s objectivity to establish the certificate is compromised in fact
or in appearance when the Auditor for instance:
- was involved in the preparation of the Financial Statements;
- stands to benefit directly should the certificate be accepted;
- has a close relationship with any person representing the beneficiary;
- is a director, trustee or partner of the beneficiary; or
- is in any other situation that compromises his or her independence or ability to establish the certificate
impartially.
Agreed-upon procedures to be performed and standard factual findings to be confirmed by the Auditor

The European Commission reserves the right to i) provide the auditor with additional guidance regarding the procedures to be followed or the facts to be ascertained and the way in which to present them (this may include sample coverage and findings) or to ii) change the procedures, by notifying the Beneficiary in writing. The procedures carried out by the auditor to confirm the standard factual finding are listed in the table below.

If this certificate relates to a Linked Third Party, any reference here below to ‘the Beneficiary’ is to be considered as a reference to ‘the Linked Third Party’.

The ‘result’ column has three different options: ‘C’, ‘E’ and ‘N.A.’:

- ‘C’ stands for ‘confirmed’ and means that the auditor can confirm the ‘standard factual finding’ and, therefore, there is no exception to be reported.
- ‘E’ stands for ‘exception’ and means that the Auditor carried out the procedures but cannot confirm the ‘standard factual finding’, or that the Auditor was not able to carry out a specific procedure (e.g. because it was impossible to reconcile key information or data were unavailable).
- ‘N.A.’ stands for ‘not applicable’ and means that the Finding did not have to be examined by the Auditor and the related Procedure(s) did not have to be carried out. The reasons of the non-application of a certain Finding must be obvious i.e. i) if no cost was declared under a certain category then the related Finding(s) and Procedure(s) are not applicable; ii) if the condition set to apply certain Procedure(s) are not met then the related Finding(s) and Procedure(s) are not applicable. For instance, for ‘beneficiaries with accounts established in a currency other than the euro’ the Procedure related to ‘beneficiaries with accounts established in euro’ is not applicable. Similarly, if no additional remuneration is paid, the related Finding(s) and Procedure(s) for additional remuneration are not applicable.

<table>
<thead>
<tr>
<th>Ref</th>
<th>Procedures</th>
<th>Standard factual finding</th>
<th>Result (C / E / N.A.)</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>ACTUAL PERSONNEL COSTS AND UNIT COSTS CALCULATED BY THE BENEFICIARY IN ACCORDANCE WITH ITS USUAL COST ACCOUNTING PRACTICE</td>
<td></td>
<td></td>
</tr>
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<td></td>
<td>The Auditor draws a sample of persons whose costs were declared in the Financial Statement(s) to carry out the procedures indicated in the consecutive points of this section A. (The sample should be selected randomly so that it is representative. Full coverage is required if there are fewer than 10 people (including employees, natural persons working under a direct contract and personnel seconded by a third party), otherwise the sample should have a minimum of 10 people, or 10% of the total, whichever number is the highest) The Auditor sampled ______ people out of the total of ______ people.</td>
<td></td>
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</tr>
</tbody>
</table>
### A.1 PERSONNEL COSTS

For the persons included in the sample and working under an employment contract or equivalent act (general procedures for individual actual personnel costs and personnel costs declared as unit costs)

To confirm standard factual findings 1-5 listed in the next column, the Auditor reviewed following information/documents provided by the Beneficiary:

- a list of the persons included in the sample indicating the period(s) during which they worked for the action, their position (classification or category) and type of contract;
- the payslips of the employees included in the sample;
- reconciliation of the personnel costs declared in the Financial Statement(s) with the accounting system (project accounting and general ledger) and payroll system;
- information concerning the employment status and employment conditions of personnel included in the sample, in particular their employment contracts or equivalent;
- the Beneficiary’s usual policy regarding payroll matters (e.g. salary policy, overtime policy, variable pay);
- applicable national law on taxes, labour and social security and
- any other document that supports the personnel costs declared.

The Auditor also verified the eligibility of all components of the retribution (see Article 6 GA) and recalculated the personnel costs for employees included in the sample.

### Further procedures if ‘additional remuneration’ is paid

To confirm standard factual findings 6-9 listed in the next column, the Auditor:

- reviewed relevant documents provided by the Beneficiary (legal form, legal/statutory

<table>
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</table>
| A.1 | **PERSONNEL COSTS**  
For the persons included in the sample and working under an employment contract or equivalent act (general procedures for individual actual personnel costs and personnel costs declared as unit costs)  
To confirm standard factual findings 1-5 listed in the next column, the Auditor reviewed following information/documents provided by the Beneficiary:

- a list of the persons included in the sample indicating the period(s) during which they worked for the action, their position (classification or category) and type of contract;
- the payslips of the employees included in the sample;
- reconciliation of the personnel costs declared in the Financial Statement(s) with the accounting system (project accounting and general ledger) and payroll system;
- information concerning the employment status and employment conditions of personnel included in the sample, in particular their employment contracts or equivalent;
- the Beneficiary’s usual policy regarding payroll matters (e.g. salary policy, overtime policy, variable pay);
- applicable national law on taxes, labour and social security and
- any other document that supports the personnel costs declared.

The Auditor also verified the eligibility of all components of the retribution (see Article 6 GA) and recalculated the personnel costs for employees included in the sample. | 1) The employees were i) directly hired by the Beneficiary in accordance with its national legislation, ii) under the Beneficiary’s sole technical supervision and responsibility and iii) remunerated in accordance with the Beneficiary’s usual practices. | (C / E / N.A.) |
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<tbody>
<tr>
<td>1)</td>
<td>The employees were i) directly hired by the Beneficiary in accordance with its national legislation, ii) under the Beneficiary’s sole technical supervision and responsibility and iii) remunerated in accordance with the Beneficiary’s usual practices.</td>
<td>2) Personnel costs were recorded in the Beneficiary's accounts/payroll system.</td>
<td>(C / E / N.A.)</td>
</tr>
<tr>
<td>2)</td>
<td>Personnel costs were recorded in the Beneficiary's accounts/payroll system.</td>
<td>3) Costs were adequately supported and reconciled with the accounts and payroll records.</td>
<td>(C / E / N.A.)</td>
</tr>
<tr>
<td>3)</td>
<td>Costs were adequately supported and reconciled with the accounts and payroll records.</td>
<td>4) Personnel costs did not contain any ineligible elements.</td>
<td>(C / E / N.A.)</td>
</tr>
<tr>
<td>4)</td>
<td>Personnel costs did not contain any ineligible elements.</td>
<td>5) There were no discrepancies between the personnel costs charged to the action and the costs recalculated by the Auditor.</td>
<td>(C / E / N.A.)</td>
</tr>
<tr>
<td>5)</td>
<td>There were no discrepancies between the personnel costs charged to the action and the costs recalculated by the Auditor.</td>
<td>6) The Beneficiary paying “additional remuneration” was a non-profit legal entity.</td>
<td>(C / E / N.A.)</td>
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</table>
obligations, the Beneficiary’s usual policy on additional remuneration, criteria used for its calculation, the Beneficiary’s usual remuneration practice for projects funded under national funding schemes…);

- recalculated the amount of additional remuneration eligible for the action based on the supporting documents received (full-time or part-time work, exclusive or non-exclusive dedication to the action, usual remuneration paid for projects funded by national schemes) to arrive at the applicable FTE/year and pro-rata rate (see data collected in the course of carrying out the procedures under A.2 ‘Productive hours’ and A.4 ‘Time recording system’).

‘ADDITIONAL REMUNERATION’ MEANS ANY PART OF THE REMUNERATION WHICH EXCEEDS WHAT THE PERSON WOULD BE PAID FOR TIME WORKED IN PROJECTS FUNDED BY NATIONAL SCHEMES.

**IF ANY PART OF THE REMUNERATION PAID TO THE EMPLOYEE QUALIFIES AS “ADDITIONAL REMUNERATION” AND IS ELIGIBLE UNDER THE PROVISIONS OF ARTICLE 6.2.A.1, THIS CAN BE CHARGED AS ELIGIBLE COST TO THE ACTION UP TO THE FOLLOWING AMOUNT:**

- **(A) **IF THE PERSON WORKS FULL TIME AND EXCLUSIVELY ON THE ACTION DURING THE FULL YEAR: UP TO EUR 8,000/YEAR;

- **(B) **IF THE PERSON WORKS EXCLUSIVELY ON THE ACTION BUT NOT FULL-TIME OR NOT FOR THE FULL YEAR: UP TO THE CORRESPONDING PRO-RATA AMOUNT OF EUR 8,000, OR

- **(C) **IF THE PERSON DOES NOT WORK EXCLUSIVELY ON THE ACTION: UP TO A PRO-RATA AMOUNT CALCULATED IN ACCORDANCE TO ARTICLE 6.2.A.1.

**Additional procedures in case “unit costs calculated by the Beneficiary in accordance with its usual cost accounting practices” is applied:**

Apart from carrying out the procedures indicated above to confirm standard factual findings 1-5 and, if applicable, also 6-9, the Auditor carried out following procedures to confirm standard
**Procedures**

- obtained a description of the Beneficiary's usual cost accounting practice to calculate unit costs;
- reviewed whether the Beneficiary's usual cost accounting practice was applied for the Financial Statements subject of the present CFS;
- verified the employees included in the sample were charged under the correct category (in accordance with the criteria used by the Beneficiary to establish personnel categories) by reviewing the contract/HR-record or analytical accounting records;
- verified that there is no difference between the total amount of personnel costs used in calculating the cost per unit and the total amount of personnel costs recorded in the statutory accounts;
- verified whether actual personnel costs were adjusted on the basis of budgeted or estimated elements and, if so, verified whether those elements used are actually relevant for the calculation, objective and supported by documents.

For natural persons included in the sample and working with the Beneficiary under a direct contract other than an employment contract, such as consultants (no subcontractors).

To confirm standard factual findings 14-17 listed in the next column the Auditor reviewed following information/documents provided by the Beneficiary:

- the contracts, especially the cost, contract duration, work description, place of work, ownership of the results and reporting obligations to the Beneficiary;
- the employment conditions of staff in the same category to compare costs and;
- any other document that supports the costs declared and its registration (e.g. invoices, accounting records, etc.).

**Standard factual finding**

- used in all H2020 actions.
- 11) The employees were charged under the correct category.
- 12) Total personnel costs used in calculating the unit costs were consistent with the expenses recorded in the statutory accounts.
- 13) Any estimated or budgeted element used by the Beneficiary in its unit-cost calculation were relevant for calculating personnel costs and corresponded to objective and verifiable information.
- 14) The natural persons worked under conditions similar to those of an employee, in particular regarding the way the work is organised, the tasks that are performed and the premises where they are performed.
- 15) The results of work carried out belong to the Beneficiary, or, if not, the Beneficiary has obtained all necessary rights to fulfil its obligations as if those
<table>
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<th>Result (C / E / N.A.)</th>
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<td></td>
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<td>results were generated by itself.</td>
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<tr>
<td>16)</td>
<td>Their costs were not significantly different from those for staff who performed similar tasks under an employment contract with the Beneficiary.</td>
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<td>17)</td>
<td>The costs were supported by audit evidence and registered in the accounts.</td>
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<tr>
<td>18)</td>
<td>Seconded personnel reported to the Beneficiary and worked on the Beneficiary’s premises (unless otherwise agreed with the Beneficiary).</td>
<td></td>
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<tr>
<td>19)</td>
<td>The results of work carried out belong to the Beneficiary, or, if not, the Beneficiary has obtained all necessary rights to fulfil its obligations as if those results were generated by itself.</td>
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<td></td>
<td>If personnel is seconded against payment:</td>
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<td>20)</td>
<td>The costs declared were supported with documentation and recorded in the</td>
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</table>

For personnel seconded by a third party and included in the sample (not subcontractors)

To confirm standard factual findings 18-21 listed in the next column, the Auditor reviewed following information/documents provided by the Beneficiary:

- their secondment contract(s) notably regarding costs, duration, work description, place of work and ownership of the results;
- if there is reimbursement by the Beneficiary to the third party for the resource made available (in-kind contribution against payment): any documentation that supports the costs declared (e.g. contract, invoice, bank payment, and proof of registration in its accounting/payroll, etc.) and reconciliation of the Financial Statement(s) with the accounting system (project accounting and general ledger) as well as any proof that the amount invoiced by the third party did not include any profit;
- if there is no reimbursement by the Beneficiary to the third party for the resource made available (in-kind contribution free of charge): a proof of the actual cost borne by the Third Party for the resource made available free of charge to the Beneficiary such as a statement of costs incurred by the Third Party and proof of the registration in the Third Party’s accounting/payroll;
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<td></td>
<td>o any other document that supports the costs declared (e.g. invoices, etc.).</td>
<td>Beneficiary’s accounts. The third party did not include any profit.</td>
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<td>If personnel is seconded free of charge:</td>
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<td>21) The costs declared did not exceed the third party’s cost as recorded in the accounts of the third party and were supported with documentation.</td>
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<td>22) The Beneficiary applied method [choose one option and delete the others]</td>
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<td>[A: 1720 hours]</td>
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<td></td>
<td></td>
<td>[B: the ‘total number of hours worked’]</td>
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<tr>
<td></td>
<td></td>
<td>[C: ‘standard annual productive hours’ used correspond to usual accounting practices]</td>
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<tr>
<td>A.2</td>
<td>PRODUCTIVE HOURS</td>
<td>23) Productive hours were calculated annually.</td>
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<tr>
<td></td>
<td>To confirm standard factual findings 22-27 listed in the next column, the Auditor reviewed relevant documents, especially national legislation, labour agreements and contracts and time records of the persons included in the sample, to verify that:</td>
<td>24) For employees not working full-time the full-time equivalent (FTE) ratio was correctly applied.</td>
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<td>o the annual productive hours applied were calculated in accordance with one of the methods described below,</td>
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<tr>
<td></td>
<td>o the full-time equivalent (FTEs) ratios for employees not working full-time were correctly calculated.</td>
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<td></td>
<td>If the Beneficiary applied method B, the auditor verified that the correctness in which the total number of hours worked was calculated and that the contracts specified the annual workable hours.</td>
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<td></td>
<td>If the Beneficiary applied method C, the auditor verified that the ‘annual productive hours’ applied when calculating the hourly rate were equivalent to at least 90% of the ‘standard annual workable hours’. The Auditor can only do this if the calculation of the standard annual workable</td>
<td></td>
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</table>
hours can be supported by records, such as national legislation, labour agreements, and contracts.

**Beneficiary’s Productive Hours’ for persons working full time shall be one of the following methods:**

A. **1720 Annual Productive Hours (pro-rata for persons not working full-time)**

B. **The total number of hours worked by the person for the Beneficiary in the year** (this method is also referred to as ‘total number of hours worked’ in the next column). The calculation of the total number of hours worked was done as follows: annual workable hours of the person according to the employment contract, applicable labour agreement or national law plus overtime worked minus absences (such as sick leave or special leave).

C. **The standard number of annual hours generally applied by the Beneficiary for its personnel in accordance with its usual cost accounting practices** (this method is also referred to as ‘standard annual productive hours’ in the next column). This number must be at least 90% of the standard annual workable hours.

‘Annual workable hours’ means the period during which the personnel must be working, at the employer’s disposal and carrying out his/her activity or duties under the employment contract, applicable collective labour agreement or national working time legislation.

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<th>Standard factual finding</th>
<th>Result</th>
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<tr>
<td></td>
<td></td>
<td>If the Beneficiary applied method B.</td>
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<tr>
<td>25)</td>
<td>The calculation of the number of ‘annual workable hours’, overtime and absences was verifiable based on the documents provided by the Beneficiary.</td>
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<tr>
<td>25.1)</td>
<td>The Beneficiary calculates the hourly rates per full financial year following procedure A.3 (method B is not allowed for beneficiaries calculating hourly rates per month).</td>
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<tr>
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<td></td>
<td>If the Beneficiary applied method C.</td>
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<tr>
<td>26)</td>
<td>The calculation of the number of ‘standard annual workable hours’ was verifiable based on the documents provided by the Beneficiary.</td>
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</table>
### A.3 HOURLY PERSONNEL RATES

#### I) For unit costs calculated in accordance to the Beneficiary's usual cost accounting practice (unit costs):

If the Beneficiary has a "Certificate on Methodology to calculate unit costs" (CoMUC) approved by the Commission, the Beneficiary provides the Auditor with a description of the approved methodology and the Commission’s letter of acceptance. The Auditor verified that the Beneficiary has indeed used the methodology approved. If so, no further verification is necessary.

If the Beneficiary does not have a "Certificate on Methodology" (CoMUC) approved by the Commission, or if the methodology approved was not applied, then the Auditor:

- reviewed the documentation provided by the Beneficiary, including manuals and internal guidelines that explain how to calculate hourly rates;
- recalculated the unit costs (hourly rates) of staff included in the sample following the results of the procedures carried out in A.1 and A.2.

#### II) For individual hourly rates:

The Auditor:

- reviewed the documentation provided by the Beneficiary, including manuals and internal guidelines that explain how to calculate hourly rates;

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<tbody>
<tr>
<td>27)</td>
<td>The ‘annual productive hours’ used for calculating the hourly rate were consistent with the usual cost accounting practices of the Beneficiary and were equivalent to at least 90% of the ‘annual workable hours’.</td>
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<tr>
<td>28)</td>
<td>The Beneficiary applied [choose one option and delete the other]:</td>
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<tr>
<td></td>
<td>[Option I: “Unit costs (hourly rates) were calculated in accordance with the Beneficiary’s usual cost accounting practices”]</td>
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<td></td>
<td>[Option II: Individual hourly rates were applied]</td>
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For option I concerning unit costs and if the Beneficiary applies the methodology approved by the Commission (CoMUC):

29) The Beneficiary used the Commission-approved methodology to calculate hourly rates. It corresponded to the organisation’s usual cost accounting practices and was applied consistently for all
Grant Agreement number: [insert number] [insert acronym] [insert call identifier]

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</table>
|     | o recalculated the hourly rates of staff included in the sample (recalculation of all hourly rates if the Beneficiary uses annual rates, recalculation of three months selected randomly for every year and person if the Beneficiary uses monthly rates) following the results of the procedures carried out in A.1 and A.2;  
  o (only in case of monthly rates) confirmed that the time spent on parental leave is not deducted, and that, if parts of the basic remuneration are generated over a period longer than a month, the Beneficiary has included only the share which is generated in the month.  
  “UNIT COSTS CALCULATED BY THE BENEFICIARY IN ACCORDANCE WITH ITS USUAL COST ACCOUNTING PRACTICES”:  
  IT IS CALCULATED BY DIVIDING THE TOTAL AMOUNT OF PERSONNEL COSTS OF THE CATEGORY TO WHICH THE EMPLOYEE BELONGS VERIFIED IN LINE WITH PROCEDURE A.1 BY THE NUMBER OF FTE AND THE ANNUAL TOTAL PRODUCTIVE HOURS OF THE SAME CATEGORY CALCULATED BY THE BENEFICIARY IN ACCORDANCE WITH PROCEDURE A.2.  
  HOURLY RATE FOR INDIVIDUAL ACTUAL PERSONAL COSTS:  
  IT IS CALCULATED FOLLOWING ONE OF THE TWO OPTIONS BELOW:  
  A) [OPTION BY DEFAULT] BY DIVIDING THE ACTUAL ANNUAL AMOUNT OF PERSONNEL COSTS OF AN EMPLOYEE VERIFIED IN LINE WITH PROCEDURE A.1 BY THE NUMBER OF ANNUAL PRODUCTIVE HOURS VERIFIED IN LINE WITH PROCEDURE A.2 (FULL FINANCIAL YEAR HOURLY RATE);  
  B) BY DIVIDING THE ACTUAL MONTHLY AMOUNT OF PERSONNEL COSTS OF AN EMPLOYEE VERIFIED IN LINE WITH PROCEDURE A.1 BY 1/12 OF THE NUMBER OF ANNUAL PRODUCTIVE HOURS VERIFIED IN LINE WITH PROCEDURE A.2 (MONTHLY HOURLY RATE). | activities irrespective of the source of funding. | For option I concerning unit costs and if the Beneficiary applies a methodology not approved by the Commission:  
30) The unit costs re-calculated by the Auditor were the same as the rates applied by the Beneficiary.  
31) The individual rates re-calculated by the Auditor were the same as the rates applied by the Beneficiary.  
 31.1) The Beneficiary used only one option (per full financial year or per month) throughout each financial year examined.  
31.2) The hourly rates do not include additional remuneration. |
### A.4 TIME RECORDING SYSTEM

To verify that the time recording system ensures the fulfilment of all minimum requirements and that the hours declared for the action were correct, accurate and properly authorised and supported by documentation, the Auditor made the following checks for the persons included in the sample that declare time as worked for the action on the basis of time records:

- o description of the time recording system provided by the Beneficiary (registration, authorisation, processing in the HR-system);
- o its actual implementation;
- o time records were signed at least monthly by the employees (on paper or electronically) and authorised by the project manager or another manager;
- o the hours declared were worked within the project period;
- o there were no hours declared as worked for the action if HR-records showed absence due to holidays or sickness (further cross-checks with travels are carried out in B.1 below);
- o the hours charged to the action matched those in the time recording system.


**Result**

<table>
<thead>
<tr>
<th>Ref</th>
<th>Procedures</th>
<th>Standard factual finding</th>
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</table>
| A.4 | TIME RECORDING SYSTEM
   To verify that the time recording system ensures the fulfilment of all minimum requirements and that the hours declared for the action were correct, accurate and properly authorised and supported by documentation, the Auditor made the following checks for the persons included in the sample that declare time as worked for the action on the basis of time records:
   - o description of the time recording system provided by the Beneficiary (registration, authorisation, processing in the HR-system);
   - o its actual implementation;
   - o time records were signed at least monthly by the employees (on paper or electronically) and authorised by the project manager or another manager;
   - o the hours declared were worked within the project period;
   - o there were no hours declared as worked for the action if HR-records showed absence due to holidays or sickness (further cross-checks with travels are carried out in B.1 below);
   - o the hours charged to the action matched those in the time recording system. | 32) All persons recorded their time dedicated to the action on a **daily/ weekly/ monthly** basis using a **paper/computer-based** system. (delete the answers that are not applicable)
33) Their time-records were authorised at least monthly by the project manager or other superior.
34) Hours declared were worked within the project period and were consistent with the presences/absences recorded in HR-records.
35) There were no discrepancies between the number of hours charged to the action and the number of hours recorded.
36) The exclusive dedication is supported by a declaration signed by the Beneficiary and by any other evidence gathered. |

**O NLY THE HOURS WORKED ON THE ACTION CAN BE CHARGED. ALL WORKING TIME TO BE CHARGED SHOULD BE RECORDED THROUGHOUT THE DURATION OF THE PROJECT, ADEQUATELY SUPPORTED BY EVIDENCE OF THEIR REALITY AND RELIABILITY (SEE SPECIFIC PROVISIONS BELOW FOR PERSONS WORKING EXCLUSIVELY FOR THE ACTION WITHOUT TIME RECORDS).**

If the persons are working exclusively for the action and without time records

For the persons selected that worked exclusively for the action without time records, the Auditor verified evidence available demonstrating that they were in reality exclusively dedicated to the action and that the Beneficiary signed a declaration confirming that they have worked exclusively for the action.
**Ref** | **Procedures** | **Standard factual finding** | **Result (C / E / N.A.)**  
--- | --- | --- | ---  
B | **COSTS OF SUBCONTRACTING** | |  
B.1 | The Auditor obtained the detail/breakdown of subcontracting costs and sampled [insert number] cost items selected randomly (full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest). To confirm standard factual findings 37-41 listed in the next column, the Auditor reviewed the following for the items included in the sample:  
| o the use of subcontractors was foreseen in Annex 1;  
| o subcontracting costs were declared in the subcontracting category of the Financial Statement;  
| o supporting documents on the selection and award procedure were followed;  
| o the Beneficiary ensured best value for money (key elements to appreciate the respect of this principle are the award of the subcontract to the bid offering best price-quality ratio, under conditions of transparency and equal treatment. In case an existing framework contract was used the Beneficiary ensured it was established on the basis of the principle of best value for money under conditions of transparency and equal treatment). In particular,  
| i. if the Beneficiary acted as a contracting authority within the meaning of Directive 2004/18/EC (or 2014/24/EU) or of Directive 2004/17/EC (or 2014/25/EU), the Auditor verified that the applicable national law on public procurement was followed and that the subcontracting complied with the Terms and Conditions of the Agreement.  
| ii. if the Beneficiary did not fall under the above-mentioned category the Auditor verified that the Beneficiary followed their usual procurement rules and respected the Terms and Conditions of the Agreement.  
37) The use of claimed subcontracting costs was foreseen in Annex 1 and costs were declared in the Financial Statements under the subcontracting category.  
38) There were documents of requests to different providers, different offers and assessment of the offers before selection of the provider in line with internal procedures and procurement rules. Subcontracts were awarded in accordance with the principle of best value for money. (When different offers were not collected the Auditor explains the reasons provided by the Beneficiary under the caption “Exceptions” of the Report. The Commission will analyse this information to evaluate whether these costs might be accepted as eligible)  
39) The subcontracts were not awarded to other Beneficiaries.
For the items included in the sample the Auditor also verified that:
  o the subcontracts were not awarded to other Beneficiaries in the consortium;
  o there were signed agreements between the Beneficiary and the subcontractor;
  o there was evidence that the services were provided by subcontractor;

<table>
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<tr>
<th>Ref</th>
<th>Procedures</th>
<th>Standard factual finding</th>
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<tr>
<td></td>
<td>For the items included in the sample the Auditor also verified that:</td>
<td>of the consortium.</td>
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<tr>
<td></td>
<td>o the subcontracts were not awarded to other Beneficiaries in the consortium;</td>
<td>40) All subcontracts were supported by signed agreements between the Beneficiary and the subcontractor.</td>
</tr>
<tr>
<td></td>
<td>o there were signed agreements between the Beneficiary and the subcontractor;</td>
<td>41) There was evidence that the services were provided by the subcontractors.</td>
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<tr>
<td></td>
<td>o there was evidence that the services were provided by subcontractor;</td>
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</table>

C COSTS OF PROVIDING FINANCIAL SUPPORT TO THIRD PARTIES

C.1 The Auditor obtained the detail/breakdown of the costs of providing financial support to third parties and sampled [number] cost items selected randomly (full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 items, or 10% of the total, whichever number is highest).

The Auditor verified that the following minimum conditions were met:
  a) the maximum amount of financial support for each third party did not exceed EUR 60 000, unless explicitly mentioned in Annex 1;
  b) the financial support to third parties was agreed in Annex 1 of the Agreement and the other provisions on financial support to third parties included in Annex 1 were respected.

<table>
<thead>
<tr>
<th>Ref</th>
<th>Procedures</th>
<th>Standard factual finding</th>
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<tbody>
<tr>
<td></td>
<td>The Auditor obtained the detail/breakdown of the costs of providing financial support to third parties and sampled [number] cost items selected randomly (full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 items, or 10% of the total, whichever number is highest).</td>
<td>42) All minimum conditions were met</td>
</tr>
<tr>
<td></td>
<td>The Auditor verified that the following minimum conditions were met:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a) the maximum amount of financial support for each third party did not exceed EUR 60 000, unless explicitly mentioned in Annex 1;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b) the financial support to third parties was agreed in Annex 1 of the Agreement and the other provisions on financial support to third parties included in Annex 1 were respected.</td>
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</table>
## OTHER ACTUAL DIRECT COSTS

### D.1 COSTS OF TRAVEL AND RELATED SUBSISTENCE ALLOWANCES

The Auditor sampled **[insert number]** cost items selected randomly *(full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is the highest).*

The Auditor inspected the sample and verified that:

- travel and subsistence costs were consistent with the Beneficiary's usual policy for travel. In this context, the Beneficiary provided evidence of its normal policy for travel costs (e.g. use of first class tickets, reimbursement by the Beneficiary on the basis of actual costs, a lump sum or per diem) to enable the Auditor to compare the travel costs charged with this policy;
- travel costs are correctly identified and allocated to the action (e.g. trips are directly linked to the action) by reviewing relevant supporting documents such as minutes of meetings, workshops or conferences, their registration in the correct project account, their consistency with time records or with the dates/duration of the workshop/conference;
- no ineligible costs or excessive or reckless expenditure was declared (see Article 6.5 MGA).

43) Costs were incurred, approved and reimbursed in line with the Beneficiary's usual policy for travels.

44) There was a link between the trip and the action.

45) The supporting documents were consistent with each other regarding subject of the trip, dates, duration and reconciled with time records and accounting.

46) No ineligible costs or excessive or reckless expenditure was declared.

### D.2 DEPRECIATION COSTS FOR EQUIPMENT, INFRASTRUCTURE OR OTHER ASSETS

The Auditor sampled **[insert number]** cost items selected randomly *(full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is the highest).*

For “equipment, infrastructure or other assets” [from now on called “asset(s)”] selected in the sample the Auditor verified that:

- the assets were acquired in conformity with the Beneficiary's internal guidelines and procedures;

47) Procurement rules, principles and guides were followed.

48) There was a link between the grant agreement and the asset charged to the action.

49) The asset charged to the action was traceable to the accounting records and the underlying documents.
<p>| | |</p>
<table>
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<tbody>
<tr>
<td>50)</td>
<td>The depreciation method used to charge the asset to the action was in line with the applicable rules of the Beneficiary’s country and the Beneficiary’s usual accounting policy.</td>
</tr>
<tr>
<td>51)</td>
<td>The amount charged corresponded to the actual usage for the action.</td>
</tr>
<tr>
<td>52)</td>
<td>No ineligible costs or excessive or reckless expenditure were declared.</td>
</tr>
<tr>
<td><strong>D.3 COSTS OF OTHER GOODS AND SERVICES</strong></td>
<td></td>
</tr>
<tr>
<td>The Auditor sampled ______ cost items selected randomly (full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest).</td>
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<tr>
<td>For the purchase of goods, works or services included in the sample the Auditor verified that:</td>
<td></td>
</tr>
<tr>
<td>o the contracts did not cover tasks described in Annex 1;</td>
<td></td>
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<tr>
<td>o they were correctly identified, allocated to the proper action, entered in the accounting system (traceable to underlying documents such as purchase orders, invoices and accounting);</td>
<td></td>
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<tr>
<td>o the goods were not placed in the inventory of durable equipment;</td>
<td></td>
</tr>
<tr>
<td>o the costs charged to the action were accounted in line with the Beneficiary’s usual accounting practices;</td>
<td></td>
</tr>
<tr>
<td>o no ineligible costs or excessive or reckless expenditure were declared (see Article 6 GA).</td>
<td></td>
</tr>
<tr>
<td>In addition, the Auditor verified that these goods and services were acquired in conformity with</td>
<td></td>
</tr>
<tr>
<td>53)</td>
<td>Contracts for works or services did not cover tasks described in Annex 1.</td>
</tr>
<tr>
<td>54)</td>
<td>Costs were allocated to the correct action and the goods were not placed in the inventory of durable equipment.</td>
</tr>
<tr>
<td>55)</td>
<td>The costs were charged in line with the Beneficiary’s accounting policy and were adequately supported.</td>
</tr>
<tr>
<td>56)</td>
<td>No ineligible costs or excessive or reckless expenditure were declared. For internal invoices/charges only the cost element was charged, without any mark-ups.</td>
</tr>
</tbody>
</table>
the Beneficiary's internal guidelines and procedures, in particular:

- if Beneficiary acted as a contracting authority within the meaning of Directive 2004/18/EC (or 2014/24/EU) or of Directive 2004/17/EC (or 2014/25/EU), the Auditor verified that the applicable national law on public procurement was followed and that the procurement contract complied with the Terms and Conditions of the Agreement.
- if the Beneficiary did not fall into the category above, the Auditor verified that the Beneficiary followed their usual procurement rules and respected the Terms and Conditions of the Agreement.

For the items included in the sample the Auditor also verified that:

- the Beneficiary ensured best value for money (key elements to appreciate the respect of this principle are the award of the contract to the bid offering best price-quality ratio, under conditions of transparency and equal treatment. In case an existing framework contract was used the Auditor also verified that the Beneficiary ensured it was established on the basis of the principle of best value for money under conditions of transparency and equal treatment);

*SUCH GOODS AND SERVICES INCLUDE, FOR INSTANCE, CONSUMABLES AND SUPPLIES, DISSEMINATION (INCLUDING OPEN ACCESS), PROTECTION OF RESULTS, SPECIFIC EVALUATION OF THE ACTION IF IT IS REQUIRED BY THE AGREEMENT, CERTIFICATES ON THE FINANCIAL STATEMENTS IF THEY ARE REQUIRED BY THE AGREEMENT AND CERTIFICATES ON THE METHODOLOGY, TRANSLATIONS, REPRODUCTION.*

<table>
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<tr>
<th>57) Procurement rules, principles and guides were followed. There were documents of requests to different providers, different offers and assessment of the offers before selection of the provider in line with internal procedures and procurement rules. The purchases were made in accordance with the principle of best value for money.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(When different offers were not collected the Auditor explains the reasons provided by the Beneficiary under the caption “Exceptions” of the Report. The Commission will analyse this information to evaluate whether these costs might be accepted as eligible)</td>
</tr>
</tbody>
</table>

**D.4 AGGREGATED CAPITALISED AND OPERATING COSTS OF RESEARCH INFRASTRUCTURE**

The Auditor ensured the existence of a positive ex-ante assessment (issued by the EC Services) of the cost accounting methodology of the Beneficiary allowing it to apply the guidelines on direct costing for large research infrastructures in Horizon 2020.

| 58) The costs declared as direct costs for Large Research Infrastructures (in the appropriate line of the Financial Statement) comply with the methodology described in the positive ex-ante assessment report. |
In the cases that a positive ex-ante assessment has been issued (see the standard factual findings 58-59 on the next column),

The Auditor ensured that the beneficiary has applied consistently the methodology that is explained and approved in the positive ex ante assessment;

In the cases that a positive ex-ante assessment has NOT been issued (see the standard factual findings 60 on the next column),

The Auditor verified that no costs of Large Research Infrastructure have been charged as direct costs in any costs category;

In the cases that a draft ex-ante assessment report has been issued with recommendation for further changes (see the standard factual findings 60 on the next column),

- The Auditor followed the same procedure as above (when a positive ex-ante assessment has NOT yet been issued) and paid particular attention (testing reinforced) to the cost items for which the draft ex-ante assessment either rejected the inclusion as direct costs for Large Research Infrastructures or issued recommendations.

59) Any difference between the methodology applied and the one positively assessed was extensively described and adjusted accordingly.

60) The direct costs declared were free from any indirect costs items related to the Large Research Infrastructure.

D.5 Costs of internally invoiced goods and services

The Auditor sampled cost items selected randomly (full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest).

To confirm standard factual findings 61-65 listed in the next column, the Auditor:

- obtained a description of the Beneficiary's usual cost accounting practice to calculate costs of internally invoiced goods and services (unit costs);
- reviewed whether the Beneficiary's usual cost accounting practice was applied for the Financial Statements subject of the present CFS;
- ensured that the methodology to calculate unit costs is being used in a consistent manner, based on objective criteria, regardless of the source of funding;
- verified that any ineligible items or any costs claimed under other budget categories, in particular indirect costs, have not been taken into account when calculating the costs of

61) The costs of internally invoiced goods and services included in the Financial Statement were calculated in accordance with the Beneficiary's usual cost accounting practice.

62) The cost accounting practices used to calculate the costs of internally invoiced goods and services were applied by the Beneficiary in a consistent manner based on objective criteria regardless of the source of funding.

63) The unit cost is calculated using the actual costs for the good or service recorded in the Beneficiary’s accounts, excluding any ineligible cost or costs included in other
internally invoiced goods and services (see Article 6 GA);

- verified whether actual costs of internally invoiced goods and services were adjusted on the basis of budgeted or estimated elements and, if so, verified whether those elements used are actually relevant for the calculation, and correspond to objective and verifiable information.
- verified that any costs of items which are not directly linked to the production of the invoiced goods or service (e.g. supporting services like cleaning, general accountancy, administrative support, etc. not directly used for production of the good or service) have not been taken into account when calculating the costs of internally invoiced goods and services.
- verified that any costs of items used for calculating the costs internally invoiced goods and services are supported by audit evidence and registered in the accounts.

<table>
<thead>
<tr>
<th>E</th>
<th>USE OF EXCHANGE RATES</th>
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<tbody>
<tr>
<td>E.1</td>
<td>a) For Beneficiaries with accounts established in a currency other than euros</td>
</tr>
</tbody>
</table>
| | The Auditor sampled ______ cost items selected randomly and verified that the exchange rates used for converting other currencies into euros were in accordance with the following rules established in the Agreement (full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest):

    **Costs recorded in the accounts in a currency other than euro shall be converted into euro at the average of the daily exchange rates published in the C series of Official Journal of the European Union (https://www.ecb.int/stats/exchange/eurofxref/html/index.en.html), determined over the corresponding reporting period.**

    **If no daily euro exchange rate is published in the Official Journal of the European Union for the currency in question, conversion shall be made at the average of the monthly accounting rates established by the Commission and published on its website (http://ec.europa.eu/budget/contracts_grants/info_contracts/inforeuro/inforeuro_en.cfm),** |

<p>| | budget categories. |
| | 64) The unit cost excludes any costs of items which are not directly linked to the production of the invoiced goods or service. |
| | 65) The costs items used for calculating the actual costs of internally invoiced goods and services were relevant, reasonable and correspond to objective and verifiable information. |
| | 66) The exchange rates used to convert other currencies into Euros were in accordance with the rules established of the Grant Agreement and there was no difference in the final figures. |</p>
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<tr>
<th>DETERMINED OVER THE CORRESPONDING REPORTING PERIOD.</th>
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</table>

b) For Beneficiaries with accounts established in euros

The Auditor sampled ______ cost items selected randomly and verified that the exchange rates used for converting other currencies into euros were in accordance with the following rules established in the Agreement

(full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest):

**COSTS INCURRED IN ANOTHER CURRENCY SHALL BE CONVERTED INTO EURO BY APPLYING THE BENEFICIARY’S USUAL ACCOUNTING PRACTICES.**

67) The Beneficiary applied its usual accounting practices.

[legal name of the audit firm]
[name and function of an authorised representative]
[dd Month yyyy]

<Signature of the Auditor>
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TERMS OF REFERENCE FOR AN AUDIT ENGAGEMENT FOR A METHODOLOGY CERTIFICATE IN CONNECTION WITH ONE OR MORE GRANT AGREEMENTS FINANCED UNDER THE HORIZON 2020 RESEARCH AND INNOVATION FRAMEWORK PROGRAMME

INDEPENDENT REPORT OF FACTUAL FINDINGS ON THE METHODOLOGY CONCERNING GRANT AGREEMENTS FINANCED UNDER THE HORIZON 2020 RESEARCH AND INNOVATION FRAMEWORK PROGRAMME
Terms of reference for an audit engagement for a methodology certificate in connection with one or more grant agreements financed under the Horizon 2020 Research and Innovation Framework Programme

This document sets out the ‘Terms of Reference (ToR)’ under which

[OPTION 1: [insert name of the beneficiary] (‘the Beneficiary’) ] [OPTION 2: [insert name of the linked third party] (‘the Linked Third Party’), third party linked to the Beneficiary [insert name of the beneficiary] (‘the Beneficiary’) ]

agrees to engage

[insert legal name of the auditor] (‘the Auditor’)

to produce an independent report of factual findings (‘the Report’) concerning the [Beneficiary’s] [Linked Third Party’s] usual accounting practices for calculating and claiming direct personnel costs declared as unit costs (‘the Methodology’) in connection with grant agreements financed under the Horizon 2020 Research and Innovation Framework Programme.

The procedures to be carried out for the assessment of the methodology will be based on the grant agreement(s) detailed below:

[title and number of the grant agreement(s)] (‘the Agreement(s)’)

The Agreement(s) has(have) been concluded between the Beneficiary and [OPTION 1: the European Union, represented by the European Commission (‘the Commission’)] [OPTION 2: the European Atomic Energy Community (Euratom,) represented by the European Commission (‘the Commission’)] [OPTION 3: the [Research Executive Agency (REA)] [European Research Council Executive Agency (ERCEA)] [Innovation and Networks Executive Agency (INEA)] [Executive Agency for Small and Medium-sized Enterprises (EASME)] (‘the Agency’), under the powers delegated by the European Commission (‘the Commission’).

The [Commission] [Agency] is mentioned as a signatory of the Agreement with the Beneficiary only. The [European Union] [Euratom] [Agency] is not a party to this engagement.

1.1 Subject of the engagement

According to Article 18.1.2 of the Agreement, beneficiaries [and linked third parties] that declare direct personnel costs as unit costs calculated in accordance with their usual cost accounting practices may submit to the [Commission] [Agency], for approval, a certificate on the methodology (‘CoMUC’) stating that there are adequate records and documentation to prove that their cost accounting practices used comply with the conditions set out in Point A of Article 6.2.

The subject of this engagement is the CoMUC which is composed of two separate documents:

- the Terms of Reference (‘the ToR’) to be signed by the [Beneficiary] [Linked Third Party] and the Auditor;
- the Auditor’s Independent Report of Factual Findings (‘the Report’) issued on the Auditor’s letterhead, dated, stamped and signed by the Auditor which includes; the standard statements (‘the Statements’) evaluated and signed by the [Beneficiary] [Linked Third Party], the agreed-upon procedures (‘the Procedures’) performed by the Auditor and the standard factual findings
(‘the Findings’) assessed by the Auditor. The Statements, Procedures and Findings are summarised in the table that forms part of the Report.

The information provided through the Statements, the Procedures and the Findings will enable the Commission to draw conclusions regarding the existence of the [Beneficiary’s] [Linked Third Party’s] usual cost accounting practice and its suitability to ensure that direct personnel costs claimed on that basis comply with the provisions of the Agreement. The Commission draws its own conclusions from the Report and any additional information it may require.

1.2 Responsibilities

The parties to this agreement are the [Beneficiary] [Linked Third Party] and the Auditor.

The [Beneficiary] [Linked Third Party]:
- is responsible for preparing financial statements for the Agreement(s) (‘the Financial Statements’) in compliance with those Agreements;
- is responsible for providing the Financial Statement(s) to the Auditor and enabling the Auditor to reconcile them with the [Beneficiary’s] [Linked Third Party’s] accounting and bookkeeping system and the underlying accounts and records. The Financial Statement(s) will be used as a basis for the procedures which the Auditor will carry out under this ToR;
- is responsible for its Methodology and liable for the accuracy of the Financial Statement(s);
- is responsible for endorsing or refuting the Statements indicated under the heading ‘Statements to be made by the Beneficiary/Linked Third Party’ in the first column of the table that forms part of the Report;
- must provide the Auditor with a signed and dated representation letter;
- accepts that the ability of the Auditor to carry out the Procedures effectively depends upon the [Beneficiary] [Linked Third Party] providing full and free access to the [Beneficiary’s] [Linked Third Party’s] staff and to its accounting and other relevant records.

The Auditor:
- [Option 2 if the Beneficiary or Linked Third Party has an independent Public Officer: is a competent and independent Public Officer for which the relevant national authorities have established the legal capacity to audit the Beneficiary].
- [Option 3 if the Beneficiary or Linked Third Party is an international organisation: is an [internal] [external] auditor in accordance with the internal financial regulations and procedures of the international organisation].

The Auditor:
- must be independent from the Beneficiary [and the Linked Third Party], in particular, it must not have been involved in preparing the Beneficiary’s [and Linked Third Party’s] Financial Statement(s);
- must plan work so that the Procedures may be carried out and the Findings may be assessed;
- must adhere to the Procedures laid down and the compulsory report format;
- must carry out the engagement in accordance with these ToR;
- must document matters which are important to support the Report;
- must base its Report on the evidence gathered;
- must submit the Report to the [Beneficiary] [Linked Third Party].
The Commission sets out the Procedures to be carried out and the Findings to be endorsed by the Auditor. The Auditor is not responsible for their suitability or pertinence. As this engagement is not an assurance engagement the Auditor does not provide an audit opinion or a statement of assurance.

1.3 Applicable Standards

The Auditor must comply with these Terms of Reference and with¹:

- the International Standard on Related Services (‘ISRS’) 4400 *Engagements to perform Agreed-upon Procedures regarding Financial Information* as issued by the International Auditing and Assurance Standards Board (IAASB);
- the *Code of Ethics for Professional Accountants* issued by the International Ethics Standards Board for Accountants (IESBA). Although ISRS 4400 states that independence is not a requirement for engagements to carry out agreed-upon procedures, the Commission requires that the Auditor also complies with the Code’s independence requirements.

The Auditor’s Report must state that there was no conflict of interests in establishing this Report between the Auditor and the Beneficiary *and the Linked Third Party* that could have a bearing on the Report, and must specify – if the service is invoiced - the total fee paid to the Auditor for providing the Report.

1.4 Reporting

The Report must be written in the language of the Agreement (see Article 20.7 of the Agreement).

Under Article 22 of the Agreement, the Commission, *the Agency*, the European Anti-Fraud Office and the Court of Auditors have the right to audit any work that is carried out under the action and for which costs are declared from *the European Union* [*Euratom*] budget. This includes work related to this engagement. The Auditor must provide access to all working papers related to this assignment if the Commission*, the Agency*, the European Anti-Fraud Office or the European Court of Auditors requests them.

1.5 Timing

The Report must be provided by *dd Month yyyy*.

1.6 Other Terms

*The [Beneficiary] [Linked Third Party] and the Auditor can use this section to agree other specific terms, such as the Auditor’s fees, liability, applicable law, etc. Those specific terms must not contradict the terms specified above.*

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¹ Supreme Audit Institutions applying INTOSAI-standards may carry out the Procedures according to the corresponding International Standards of Supreme Audit Institutions and code of ethics issued by INTOSAI instead of the International Standard on Related Services (‘ISRS’) 4400 and the Code of Ethics for Professional Accountants issued by the IAASB and the IESBA.
Independent report of factual findings on the methodology concerning grant agreements financed under the Horizon 2020 Research and Innovation Framework Programme

(To be printed on letterhead paper of the auditor)

To
[ name of contact person(s)], [Position]
[[Beneficiary’s] [Linked Third Party’s] name]
[ Address]
[ dd Month yyyy]

Dear [Name of contact person(s)],

As agreed under the terms of reference dated [dd Month yyyy]
with [OPTION 1: [insert name of the beneficiary] (‘the Beneficiary’)] [OPTION 2: [insert name of the linked third party] (‘the Linked Third Party’), third party linked to the Beneficiary [insert name of the beneficiary] (‘the Beneficiary’),

we

[ name of the auditor] (‘the Auditor’),

established at
[ full address/city/state/province/country],

represented by

[name and function of an authorised representative],

have carried out the agreed-upon procedures (‘the Procedures’) and provide hereby our Independent Report of Factual Findings (‘the Report’), concerning the [Beneficiary’s] [Linked Third Party’s] usual accounting practices for calculating and declaring direct personnel costs declared as unit costs (‘the Methodology’).

You requested certain procedures to be carried out in connection with the grant(s)

[title and number of the grant agreement(s)] (‘the Agreement(s)’).

The Report

Our engagement was carried out in accordance with the terms of reference (‘the ToR’) appended to this Report. The Report includes: the standard statements (‘the Statements’) made by the [Beneficiary] [Linked Third Party], the agreed-upon procedures (‘the Procedures’) carried out and the standard factual findings (‘the Findings’) confirmed by us.

The engagement involved carrying out the Procedures and assessing the Findings and the documentation requested appended to this Report, the results of which the Commission uses to draw conclusions regarding the acceptability of the Methodology applied by the [Beneficiary] [Linked Third Party].
The Report covers the methodology used from [dd Month yyyy]. In the event that the [Beneficiary] [Linked Third Party] changes this methodology, the Report will not be applicable to any Financial Statement\(^1\) submitted thereafter.

The scope of the Procedures and the definition of the standard statements and findings were determined solely by the Commission. Therefore, the Auditor is not responsible for their suitability or pertinence.

Since the Procedures carried out constitute neither an audit nor a review made in accordance with International Standards on Auditing or International Standards on Review Engagements, we do not give a statement of assurance on the costs declared on the basis of the [Beneficiary’s] [Linked Third Party’s] Methodology. Had we carried out additional procedures or had we performed an audit or review in accordance with these standards, other matters might have come to its attention and would have been included in the Report.

Exceptions

Apart from the exceptions listed below, the [Beneficiary] [Linked Third Party] agreed with the standard Statements and provided the Auditor all the documentation and accounting information needed by the Auditor to carry out the requested Procedures and corroborate the standard Findings.

<table>
<thead>
<tr>
<th>List here any exception and add any information on the cause and possible consequences of each exception, if known. If the exception is quantifiable, also indicate the corresponding amount.</th>
</tr>
</thead>
</table>

\[Explanation of possible exceptions in the form of examples (to be removed from the Report):\]

- i. the [Beneficiary] [Linked Third Party] did not agree with the standard Statement number … because…;
- ii. the Auditor could not carry out the procedure … established because …. (e.g. due to the inability to reconcile key information or the unavailability or inconsistency of data);
- iii. the Auditor could not confirm or corroborate the standard Finding number … because ….

Remarks

We would like to add the following remarks relevant for the proper understanding of the Methodology applied by the [Beneficiary] [Linked Third Party] or the results reported:

<table>
<thead>
<tr>
<th>Example (to be removed from the Report):</th>
</tr>
</thead>
</table>

Regarding the methodology applied to calculate hourly rates …

Regarding standard Finding 15 it has to be noted that …

The [Beneficiary] [Linked Third Party] explained the deviation from the benchmark statement XXIV concerning time recording for personnel with no exclusive dedication to the action in the following manner:

Annexes

Please provide the following documents to the auditor and annex them to the report when submitting this CoMUC to the Commission:

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\(^1\) Financial Statement in this context refers solely to Annex 4 of the Agreement by which the Beneficiary declares costs under the Agreement.
1. Brief description of the methodology for calculating personnel costs, productive hours and hourly rates;
2. Brief description of the time recording system in place;
3. An example of the time records used by the [Beneficiary] [Linked Third Party];
4. Description of any budgeted or estimated elements applied, together with an explanation as to why they are relevant for calculating the personnel costs and how they are based on objective and verifiable information;
5. A summary sheet with the hourly rate for direct personnel declared by the [Beneficiary] [Linked Third Party] and recalculated by the Auditor for each staff member included in the sample (the names do not need to be reported);
6. A comparative table summarising for each person selected in the sample a) the time claimed by the [Beneficiary] [Linked Third Party] in the Financial Statement(s) and b) the time according to the time record verified by the Auditor;
7. A copy of the letter of representation provided to the Auditor.

Use of this Report

This Report has been drawn up solely for the purpose given under Point 1.1 Reasons for the engagement.

The Report:
- is confidential and is intended to be submitted to the Commission by the [Beneficiary] [Linked Third Party] in connection with Article 18.1.2 of the Agreement;
- may not be used by the [Beneficiary] [Linked Third Party] or by the Commission for any other purpose, nor distributed to any other parties;
- may be disclosed by the Commission only to authorised parties, in particular the European Anti-Fraud Office (OLAF) and the European Court of Auditors.
- relates only to the usual cost accounting practices specified above and does not constitute a report on the Financial Statements of the [Beneficiary] [Linked Third Party].

No conflict of interest exists between the Auditor and the Beneficiary [and the Linked Third Party] that could have a bearing on the Report. The total fee paid to the Auditor for producing the Report was EUR [amount] (including EUR [amount] of deductible VAT).

We look forward to discussing our Report with you and would be pleased to provide any further information or assistance which may be required.

Yours sincerely

[legal name of the Auditor]
[name and title of the authorised representative]
[dd Month yyyy]
Signature of the Auditor

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2 A conflict of interest arises when the Auditor's objectivity to establish the certificate is compromised in fact or in appearance when the Auditor for instance:
- was involved in the preparation of the Financial Statements;
- stands to benefit directly should the certificate be accepted;
- has a close relationship with any person representing the beneficiary;
- is a director, trustee or partner of the beneficiary; or
- is in any other situation that compromises his or her independence or ability to establish the certificate impartially.
Statements to be made by the Beneficiary/Linked Third Party (‘the Statements’) and Procedures to be carried out by the Auditor (‘the Procedures’) and standard factual findings (‘the Findings’) to be confirmed by the Auditor

The Commission reserves the right to provide the auditor with guidance regarding the Statements to be made, the Procedures to be carried out or the Findings to be ascertained and the way in which to present them. The Commission reserves the right to vary the Statements, Procedures or Findings by written notification to the Beneficiary/Linked Third Party to adapt the procedures to changes in the grant agreement(s) or to any other circumstances.

If this methodology certificate relates to the Linked Third Party’s usual accounting practices for calculating and claiming direct personnel costs declared as unit costs any reference here below to ‘the Beneficiary’ is to be considered as a reference to ‘the Linked Third Party’.

<table>
<thead>
<tr>
<th>Please explain any discrepancies in the body of the Report.</th>
<th>Procedures to be carried out and Findings to be confirmed by the Auditor</th>
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</thead>
<tbody>
<tr>
<td><strong>Statements to be made by Beneficiary</strong></td>
<td><strong>Procedure:</strong></td>
</tr>
<tr>
<td>A. Use of the Methodology</td>
<td>✓ The Auditor checked these dates against the documentation the Beneficiary has provided.</td>
</tr>
<tr>
<td>I. The cost accounting practice described below has been in use since [dd Month yyyy].</td>
<td><strong>Factual finding:</strong></td>
</tr>
<tr>
<td>II. The next planned alteration to the methodology used by the Beneficiary will be from [dd Month yyyy].</td>
<td>1. The dates provided by the Beneficiary were consistent with the documentation.</td>
</tr>
<tr>
<td><strong>B. Description of the Methodology</strong></td>
<td><strong>Procedure:</strong></td>
</tr>
<tr>
<td>III. The methodology to calculate unit costs is being used in a consistent manner and is reflected in the relevant procedures.</td>
<td>✓ The Auditor reviewed the description, the relevant manuals and/or internal guidance documents describing the methodology.</td>
</tr>
<tr>
<td>[Please describe the methodology your entity uses to calculate personnel costs, productive hours and hourly rates, present your description to the Auditor and annex it to this certificate]</td>
<td><strong>Factual finding:</strong></td>
</tr>
<tr>
<td>[If the statement of section “B. Description of the methodology” cannot be endorsed by the Beneficiary or there is no written methodology to calculate unit costs it should be listed here below and reported as exception by the Auditor in the main Report of Factual Findings:]</td>
<td>2. The brief description was consistent with the relevant manuals, internal guidance and/or other documentary evidence the Auditor has reviewed.</td>
</tr>
<tr>
<td>“...”</td>
<td>3. The methodology was generally applied by the Beneficiary as part of its usual costs accounting practices.</td>
</tr>
</tbody>
</table>
**Please explain any discrepancies in the body of the Report.**

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<tr>
<td><strong>C. Personnel costs</strong></td>
<td><strong>Procedure:</strong></td>
</tr>
<tr>
<td><strong>General</strong></td>
<td><strong>Procedure:</strong></td>
</tr>
<tr>
<td>IV. The unit costs (hourly rates) are limited to salaries including during parental leave, social security contributions, taxes and other costs included in the remuneration required under national law and the employment contract or equivalent appointing act;</td>
<td><strong>The Auditor draws a sample of employees to carry out the procedures indicated in this section C and the following sections D to F.</strong></td>
</tr>
<tr>
<td>V. Employees are hired directly by the Beneficiary in accordance with national law, and work under its sole supervision and responsibility;</td>
<td>(The Auditor has drawn a random sample of 10 employees assigned to Horizon 2020 action(s). If fewer than 10 employees are assigned to the Horizon 2020 action(s), the Auditor has selected all employees assigned to the Horizon 2020 action(s) complemented by other employees irrespective of their assignments until he has reached 10 employees.)</td>
</tr>
<tr>
<td>VI. The Beneficiary remunerates its employees in accordance with its usual practices. This means that personnel costs are charged in line with the Beneficiary’s usual payroll policy (e.g. salary policy, overtime policy, variable pay) and no special conditions exist for employees assigned to tasks relating to the European Union or Euratom, unless explicitly provided for in the grant agreement(s);</td>
<td>For this sample:</td>
</tr>
<tr>
<td>VII. The Beneficiary allocates its employees to the relevant group/category/cost centre for the purpose of the unit cost calculation in line with the usual cost accounting practice;</td>
<td>✓ the Auditor reviewed all documents relating to personnel costs such as employment contracts, payslips, payroll policy (e.g. salary policy, overtime policy, variable pay policy), accounting and payroll records, applicable national tax, labour and social security law and any other documents corroborating the personnel costs claimed;</td>
</tr>
<tr>
<td>VIII. Personnel costs are based on the payroll system and accounting system.</td>
<td>✓ in particular, the Auditor reviewed the employment contracts of the employees in the sample to verify that:</td>
</tr>
<tr>
<td>IX. Any exceptional adjustments of actual personnel costs resulted from relevant budgeted or estimated elements and were based on objective and verifiable information. [Please describe the ‘budgeted or estimated elements’ and their relevance to personnel costs, and explain how they were reasonable and based on objective and verifiable information, present your explanation to the Auditor and annex it to this certificate].</td>
<td>i. they were employed directly by the Beneficiary in accordance with applicable national legislation;</td>
</tr>
<tr>
<td>X. Personnel costs claimed do not contain any of the following ineligible costs: costs related to return on capital; debt and debt service charges; provisions for future losses or debts; interest owed; doubtful debts; currency exchange losses; bank costs charged by the Beneficiary’s bank for transfers from the Commission/Agency; excessive or reckless expenditure; deductible VAT or costs incurred during suspension of the implementation of the action.</td>
<td>ii. they were working under the sole technical supervision and responsibility of the latter;</td>
</tr>
<tr>
<td>XI. Personnel costs were not declared under another EU or Euratom grant</td>
<td>iii. they were remunerated in accordance with the Beneficiary’s usual practices;</td>
</tr>
<tr>
<td></td>
<td>iv. they were allocated to the correct group/category/cost centre for the purposes of calculating the unit cost in line with the Beneficiary’s usual cost accounting practices;</td>
</tr>
<tr>
<td></td>
<td>✓ the Auditor verified that any ineligible items or any costs claimed under other costs categories or costs covered by other types of grant or by other grants financed from the European Union budget have not been taken into account when calculating the personnel costs;</td>
</tr>
<tr>
<td></td>
<td>✓ the Auditor numerically reconciled the total amount of personnel costs used to calculate the unit cost with the total amount of personnel costs recorded in the statutory accounts and the payroll system.</td>
</tr>
</tbody>
</table>
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<td>(including grants awarded by a Member State and financed by the EU budget and grants awarded by bodies other than the Commission/Agency for the purpose of implementing the EU or Euratom budget in the same period, unless the Beneficiary can demonstrate that the operating grant does not cover any costs of the action). If additional remuneration as referred to in the grant agreement(s) is paid</td>
<td>✓ to the extent that actual personnel costs were adjusted on the basis of budgeted or estimated elements, the Auditor carefully examined those elements and checked the information source to confirm that they correspond to objective and verifiable information;</td>
</tr>
<tr>
<td>XII. The Beneficiary is a non-profit legal entity;</td>
<td>✓ if additional remuneration has been claimed, the Auditor verified that the Beneficiary was a non-profit legal entity, that the amount was capped at EUR 8,000 per full-time equivalent and that it was reduced proportionately for employees not assigned exclusively to the action(s).</td>
</tr>
<tr>
<td>XIII. The additional remuneration is part of the beneficiary’s usual remuneration practices and paid consistently whenever the relevant work or expertise is required;</td>
<td>✓ the Auditor recalculated the personnel costs for the employees in the sample.</td>
</tr>
<tr>
<td>XIV. The criteria used to calculate the additional remuneration are objective and generally applied regardless of the source of funding;</td>
<td>Factual finding:</td>
</tr>
<tr>
<td>XV. The additional remuneration included in the personnel costs used to calculate the hourly rates for the grant agreement(s) is capped at EUR 8,000 per full-time equivalent (reduced proportionately if the employee is not assigned exclusively to the action).</td>
<td>4. All the components of the remuneration that have been claimed as personnel costs are supported by underlying documentation.</td>
</tr>
<tr>
<td></td>
<td>5. The employees in the sample were employed directly by the Beneficiary in accordance with applicable national law and were working under its sole supervision and responsibility.</td>
</tr>
<tr>
<td></td>
<td>6. Their employment contracts were in line with the Beneficiary’s usual policy;</td>
</tr>
<tr>
<td></td>
<td>7. Personnel costs were duly documented and consisted solely of salaries, social security contributions (pension contributions, health insurance, unemployment fund contributions, etc.), taxes and other statutory costs included in the remuneration (holiday pay, thirteenth month’s pay, etc.);</td>
</tr>
<tr>
<td></td>
<td>8. The totals used to calculate the personnel unit costs are consistent with those registered in the payroll and accounting records;</td>
</tr>
<tr>
<td></td>
<td>9. To the extent that actual personnel costs were adjusted on the basis of budgeted or estimated elements, those elements were relevant for calculating the personnel costs and correspond to objective and verifiable information. The budgeted or estimated elements used are: — (indicate the elements and their values).</td>
</tr>
<tr>
<td></td>
<td>10. Personnel costs contained no ineligible elements;</td>
</tr>
<tr>
<td></td>
<td>11. Specific conditions for eligibility were fulfilled when additional</td>
</tr>
</tbody>
</table>
D. Productive hours

**XVI.** The number of productive hours per full-time employee applied is [delete as appropriate]:

- **A.** 1720 productive hours per year for a person working full-time (corresponding pro-rata for persons not working full time).
- **B.** the total number of hours worked in the year by a person for the Beneficiary
- **C.** the standard number of annual hours generally applied by the beneficiary for its personnel in accordance with its usual cost accounting practices. This number must be at least 90% of the standard annual workable hours.

If method B is applied

**XVII.** The calculation of the total number of hours worked was done as follows: annual workable hours of the person according to the employment contract, applicable labour agreement or national law plus overtime worked minus absences (such as sick leave and special leave).

**XVIII.** ‘Annual workable hours’ are hours during which the personnel must be working, at the employer’s disposal and carrying out his/her activity or duties under the employment contract, applicable collective labour agreement or national working time legislation.

**XIX.** The contract (applicable collective labour agreement or national working time legislation) do specify the working time enabling to calculate the annual workable hours.

### Please explain any discrepancies in the body of the Report.

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<tbody>
<tr>
<td>remuneration was paid: a) the Beneficiary is registered in the grant agreements as a non-profit legal entity; b) it was paid according to objective criteria generally applied regardless of the source of funding used and c) remuneration was capped at EUR 8 000 per full-time equivalent (or up to up to the equivalent pro-rata amount if the person did not work on the action full-time during the year or did not work exclusively on the action).</td>
<td></td>
</tr>
</tbody>
</table>

### Procedure (same sample basis as for Section C: Personnel costs):

- The Auditor verified that the number of productive hours applied is in accordance with method A, B or C.
- The Auditor checked that the number of productive hours per full-time employee is correct.
- If method B is applied the Auditor verified i) the manner in which the total number of hours worked was done and ii) that the contract specified the annual workable hours by inspecting all the relevant documents, national legislation, labour agreements and contracts.
- If method C is applied the Auditor reviewed the manner in which the standard number of working hours per year has been calculated by inspecting all the relevant documents, national legislation, labour agreements and contracts and verified that the number of productive hours per year used for these calculations was at least 90% of the standard number of working hours per year.

### Factual finding:

**General**

- **12.** The Beneficiary applied a number of productive hours consistent with method A, B or C detailed in the left-hand column.
- **13.** The number of productive hours per year per full-time employee was accurate.

**If method B is applied**

- **14.** The number of ‘annual workable hours’, overtime and absences was...
Please explain any discrepancies in the body of the Report.

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<tr>
<td><strong>If method C is applied</strong></td>
<td><strong>E. Hourly rates</strong></td>
</tr>
<tr>
<td>XX. The standard number of productive hours per year is that of a full-time equivalent.</td>
<td>The hourly rates are correct because:</td>
</tr>
<tr>
<td>XXI. The number of productive hours per year on which the hourly rate is based i) corresponds to the Beneficiary’s usual accounting practices; ii) is at least 90% of the standard number of workable (working) hours per year.</td>
<td>XXIII. Hourly rates are correctly calculated since they result from dividing annual personnel costs by the productive hours of a given year and group (e.g. staff category or department or cost centre depending on the methodology applied) and they are in line with the statements made in section C. and D. above.</td>
</tr>
<tr>
<td>XXII. Standard workable (working) hours are hours during which personnel are at the Beneficiary’s disposal preforming the duties described in the relevant employment contract, collective labour agreement or national labour legislation. The number of standard annual workable (working) hours that the Beneficiary claims is supported by labour contracts, national legislation and other documentary evidence.</td>
<td>[If the statement of section ‘E. Hourly rates’ cannot be endorsed by the Beneficiary they should be listed here below and reported as exception by the Auditor: ]</td>
</tr>
</tbody>
</table>

**Procedures**

- The Auditor has obtained a list of all personnel rates calculated by the Beneficiary in accordance with the methodology used.
- The Auditor has obtained a list of all the relevant employees, based on which the personnel rate(s) are calculated.

For 10 employees selected at random (same sample basis as Section C: Personnel costs):

- The Auditor recalculated the hourly rates.
- The Auditor verified that the methodology applied corresponds to the usual accounting practices of the organisation and is applied consistently for all activities of the organisation on the basis of objective criteria irrespective of the source of funding.

**Factual finding:**
**Please explain any discrepancies in the body of the Report.**

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<tbody>
<tr>
<td>19. No differences arose from the recalculation of the hourly rate for the employees included in the sample.</td>
<td><strong>Procedure</strong></td>
</tr>
<tr>
<td><strong>F. Time recording</strong></td>
<td>✓ The Auditor reviewed the brief description, all relevant manuals and/or internal guidance describing the methodology used to record time.</td>
</tr>
<tr>
<td>XXIV. Time recording is in place for all persons with no exclusive dedication to one Horizon 2020 action. At least all hours worked in connection with the grant agreement(s) are registered on a daily/weekly/monthly basis [delete as appropriate] using a paper/computer-based system [delete as appropriate];</td>
<td>✓ that time records were available for all persons with not exclusive assignment to the action;</td>
</tr>
<tr>
<td>XXV. For persons exclusively assigned to one Horizon 2020 activity the Beneficiary has either signed a declaration to that effect or has put arrangements in place to record their working time;</td>
<td>✓ that time records were available for persons working exclusively for a Horizon 2020 action, or, alternatively, that a declaration signed by the Beneficiary was available for them certifying that they were working exclusively for a Horizon 2020 action;</td>
</tr>
<tr>
<td>XXVI. Records of time worked have been signed by the person concerned (on paper or electronically) and approved by the action manager or line manager at least monthly;</td>
<td>✓ that time records were signed and approved in due time and that all minimum requirements were fulfilled;</td>
</tr>
<tr>
<td>XXVII. Measures are in place to prevent staff from:</td>
<td>✓ that the persons worked for the action in the periods claimed;</td>
</tr>
<tr>
<td>i. recording the same hours twice,</td>
<td>✓ that no more hours were claimed than the productive hours used to calculate the hourly personnel rates;</td>
</tr>
<tr>
<td>ii. recording working hours during absence periods (e.g. holidays, sick leave),</td>
<td>✓ that internal controls were in place to prevent that time is recorded twice, during absences for holidays or sick leave; that more hours are claimed per person per year for Horizon 2020 actions than the number of productive hours per year used to calculate the hourly rates; that working time is recorded outside the action period;</td>
</tr>
<tr>
<td>iii. recording more than the number of productive hours per year used to calculate the hourly rates, and</td>
<td>✓ the Auditor cross-checked the information with human-resources records to verify consistency and to ensure that the internal controls have been effective. In addition, the Auditor has verified that no more hours were charged to Horizon 2020 actions per person per year than the number of productive hours per year used to calculate the hourly rates, and verified that</td>
</tr>
<tr>
<td>iv. recording hours worked outside the action period.</td>
<td></td>
</tr>
</tbody>
</table>
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<tbody>
<tr>
<td>present certificate¹.</td>
<td>no time worked outside the action period was charged to the action.</td>
</tr>
</tbody>
</table>

Factual finding:

20. The brief description, manuals and/or internal guidance on time recording provided by the Beneficiary were consistent with management reports/records and other documents reviewed and were generally applied by the Beneficiary to produce the financial statements.

21. For the random sample time was recorded or, in the case of employees working exclusively for the action, either a signed declaration or time records were available;

22. For the random sample the time records were signed by the employee and the action manager/line manager, at least monthly.

23. Working time claimed for the action occurred in the periods claimed;

24. No more hours were claimed than the number productive hours used to calculate the hourly personnel rates;

25. There is proof that the Beneficiary has checked that working time has not been claimed twice, that it is consistent with absence records and the number of productive hours per year, and that no working time has been claimed outside the action period.

26. Working time claimed is consistent with that on record at the human-resources department.

¹ The description of the time recording system must state among others information on the content of the time records, its coverage (full or action time-recording, for all personnel or only for personnel involved in H2020 actions), its degree of detail (whether there is a reference to the particular tasks accomplished), its form, periodicity of the time registration and authorisation (paper or a computer-based system; on a daily, weekly or monthly basis; signed and countersigned by whom), controls applied to prevent double-charging of time or ensure consistency with HR-records such as absences and travels as well as it information flow up to its use for the preparation of the Financial Statements.
**Please explain any discrepancies in the body of the Report.**

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<tr>
<td>[official name of the [Beneficiary] [Linked Third Party]]</td>
<td>[official name of the Auditor]</td>
</tr>
<tr>
<td>[name and title of authorised representative]</td>
<td>[name and title of authorised representative]</td>
</tr>
<tr>
<td>[dd Month yyyy]</td>
<td>[dd Month yyyy]</td>
</tr>
<tr>
<td>&lt;Signature of the [Beneficiary] [Linked Third Party]&gt;</td>
<td>&lt;Signature of the Auditor&gt;</td>
</tr>
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