Horizon 2020 Work Programme for Research & Innovation 2018-2020

'Health, demographic change and well-being' - Clinical Studies

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Clinical Studies

• Why? What?

• Template – essential information about clinical studies

• Deliverables

• Administrative status of recruitment sites

• Financial Issues: Clinical studies unit costs, Internal Invoicing
EU-funded Clinical Studies – Why?

• Bringing innovations to patients and markets
• Providing evidence to impact clinical practice and improve patient care
• Critical mass (e.g. rare diseases, stratified approaches)
• Maximise recruitment through EU or international collaboration
• Increase robustness of data
• Multidisciplinary expertise
Clinical Studies – What do we fund?
Scope, methodology, nature of the intervention, disease and target group

Hypothesis generating epidemiology studies
Hypothesis testing trials

Medical devices
Companion diagnostics
Surgery, radiotherapy, other medical interventions

Rare diseases
Non-communicable diseases
Infectious diseases
Injuries
Other health status

Pharmaceutical:
Phase I
Phase II
Phase III
Phase IV
Observational studies

Adults
Children
Elderly
Gender
Clinical Studies – What do we fund?

> 340,000 patients recruited
165 Projects, 286 CTs, € 1.1 billion

Phase I: 16%
Phase I/II: 23%
Phase II: 21%
Phase II/III: 5%
Phase III: 6%
Phase IV: 1%

Horizon 2020: more than 50% of SC1 projects include clinical studies!
Clinical studies – applicability/ definition

- A ‘clinical study’ ... any clinical research involving a substantial amount of work related to the observation of, data collection from, or diagnostic or therapeutic intervention on multiple or individual patients or study subjects. It includes but is not limited to clinical studies and clinical trials in the sense of the EU Clinical Trials Directive (2001/20/EC) and the Regulation (EU 536/2014).

- Broad, inclusive definition!
Template
Essential information about clinical studies

- providing **structured** information to experts for evaluation
- giving applicants the chance to **provide detailed information** about clinical studies without page limitations
- providing necessary information to request 'unit costs'
- **mandatory** for certain single-stage and second-stage topics (listed in the template itself) **if** a clinical study is included
  - But: no eligibility criterion, no disadvantage when information provided in other part of the proposal
  - Rather: more and more appreciated (applicants, evaluators) as an **opportunity** for structured information

1 Available under 'call documents' (http://ec.europa.eu/research/participants/data/ref/h2020/other/legal/templ/h2020_tmpl-clinical-studies_2018-2020_en.pdf) and in submission system
**Template**

**Essential information about clinical studies**

Due to the heterogeneity of clinical studies (broad, inclusive definition), not necessarily all sections of the template will be applicable to the particular study.

**BUT**

- **Completion of all relevant sections** are requested
- Short justification for omitted sections are required

**Operational feasibility** of the planned clinical study has to be demonstrated! Proposal evaluation scoring is *negatively* affected by

- Overly optimistic timelines
- Unrealistic planning in any aspect
Template
Essential information about clinical studies

NOT part of the template but key information to be provided elsewhere

• **Ethical considerations** have to be addressed in the respective section of the proposal

• **Risks and contingency plans** have to be addressed in the respective section of the proposal (part B.3.2 and table 3.2.a) ... If contingency plans are not outlined in the proposal (and the grant agreement), your grant agreement might be terminated and/or the EU contribution significantly reduced if a study cannot proceed as planned.

"Extensions of project duration can generally not be granted in H2020. Significantly delayed key study milestones (e.g. 'first patient/first visit') might lead to the termination of the grant agreement."
1.1 Identifier

1.2 Study design and endpoints

Brief description of the objectives or hypotheses and concise description of the selected study design

Description of the primary and secondary endpoints/outcome measures

Explain how patient priorities / preferences is taken into account in the proposed study

References to guidance documents relevant to the study

List treatment guidelines, methodological guidelines (e.g. Good Clinical Practice) that are applied in study design and execution
1.3 Regulatory status and activities

Clearly define the regulatory / ethics status and requirements for the study according to national and EU regulations.

Scientific advice / protocol assistance

Provide a summary of the current status, the answer(s) from the authority.

Qualification advice

Applicable in the context of new methodologies for pharmaceutical development

Provide a summary of the current status, the answer(s) from the authority.
1.4 Subjects/population(s)

Inclusion and exclusion criteria
   If there are populations specifically excluded, please justify.

Inclusion of special populations (children, elderly)

Definition of sub-populations
   Provide a summary of the current status, the answer(s) from the authority

1.5 Statistic analysis plan(ning) and power calculation

Justification of sample size, statistical methods, stopping rules, control measures for bias
1.6 Cumulative safety and efficacy information

Concise information on safety and tolerability of study interventions
For pharmaceuticals, use relevant sections of the Investigational Medicinal Product Dossier (IMPD) or in case of phase IV studies, the Summary of Product Characteristics (SmPC).

Concise information on efficacy of study interventions
For pharmaceuticals, use relevant sections of the Investigational Medicinal Product Dossier (IMPD) or in case of phase IV studies, the Summary of Product Characteristics (SmPC).
1.7 Conduct

Schedule for study conduct including timelines for key study milestones
realistic planning and timing for first patient enrolled, last patient enrolled,
last patient completed study, end of study including data analysis

Description of recruitment strategy
expected recruitment rate based on available data, contingency measures

Description and assignment of intervention(s)
methods for allocation and blinding

Study management, study monitoring, data and sample management
Include information on adverse event reporting
1.7 **Conduct** (continued)

Sponsor, coordinating centre(s) and committees

List the entities and specify their role

Study medication

If manufacturing / labelling of the study medication is required, what plans / commitments are in place

Clinical centres

criteria for site selection and indicative list of clinical centres / recruitment centres

1.8 **Orphan designation**
1. 'First study subject approvals package', for each included CS (prior to enrolment of first study subject):
   - Final version of study protocol as submitted to regulators / ethics committee(s) (no need to change deliverable if later amendments)
   - Registration number of clinical study in a WHO- or ICMJE-approved registry
     (Result posting must be possible)
   - Approvals (ethics committees and national competent authority if applicable) required for invitation / enrolment of first subject in at least one clinical centre
2. 'Midterm recruitment report', for each included CS: Deliverable to be scheduled for the time point when 50% of the study population is expected to have been recruited. The report shall include an overview of recruited subjects by study site, potential recruiting problems and, if applicable, a detailed description of implemented and planned measures to compensate delays in the study subject recruitment.
Mandatory deliverables (III)

3. **Report on status of posting results in the study registry(s), for each included CS:**
   - Report on the status of the result posting including timelines when final posting of results is scheduled after end of funding period.

Please note the obligation to post results in the registry within 12 months of primary study completion in line with the WHO 'Joint Statement on public disclosure of results from clinical trials'
Clincial centres whose contribution is limited to subject recruitment or treatment may have status of:

• Full beneficiary → always preferred!

But: if obstacles for centres to become beneficiary (or linked third party), two other options remain:

• Use of in-kind contributions provided by third parties against payment (Art. 11 MGA) – patient data are considered as in-kind contribution
• Subcontractor (Art. 13 MGA)

Please note: It is not possible to reimburse recruitment sites based on Article 10 MGA (Purchase of goods, works or services)
Administrative status of recruitment sites (II)

Use of in-kind contributions provided by third parties against payment (Art. 11 MGA)

- Third parties must be identified in DoA
- No profit, reimbursement of unit / actual costs (!)
- Requires prior agreement with beneficiary – prior to start of work, not necessarily prior to signature of GA
- Agreement might be 'ad-hoc'/specific to project
- 25% indirect costs can be claimed (by the third party itself, not by the beneficiary!) when actual or unit costs are used
Administrative status of recruitment sites (III)

**Subcontractor** (Art. 13, MGA)

- **only task (!)** must be identified in DoA
- agreed 'price per patient/subject', profit possible
- best price/quality ratio, transparency and equal treatment
- public bodies: internal rules and applicable legislation related to public procurement
- no indirect costs for beneficiary! But with 100% reimbursement rate of direct costs, no "shortfall" for linked beneficiary
Unit costs for clinical studies

- Alternative to the use of actual costs, on voluntary basis
- Calculated according to a fixed methodology \(^1\) - !not beneficiary’s own methodology!
- Requested in the proposal \(^2\) and the calculation method evaluated by the experts

**Why unit costs?**

- No need for time sheets and detailed actual costs for each patient
- Only items that are audited: Number of patients enrolled and correctness of historical costs listed


Unit costs for clinical studies

- Unit costs for clinical studies can be used by:
  - beneficiaries
  - linked third parties
  - third parties contributing in kind to the clinical study

- Can be used for any type of clinical study in any action under WP 2018-20 HEALTH

- Once the GA is signed, the choice can be changed only via an amendment \(^1\)

  if there was a change in the study protocol - e.g. due to requests from competent authorities, regulatory agencies or ethics committees, or if there was an error in the calculation, etc.

\(^1\) Commission Decision C(2016) 7553 final
Unit costs component ‘personnel costs’

Three unique and exclusive (!) personnel categories:
- Doctors
- Other medical personal
- Technical personnel

No other category possible - e.g. categories as ‘nurses’ 'study nurses' or 'pharmacists' do not exist!

‘The magic 3 numbers

Ask the accounting department of your institution for the average hourly rates in year N-1 calculated in line with the obligatory method for each of the 3 categories
‘Sequential’ unit costs for clinical studies

- Unit costs can only be claimed for patients that have completed the entire study task.
- When there are several treatments, the unit costs can be split into sequences.
- For a patient who drops out after the first treatment, only one unit cost sequence can be charged. For a patient who completes the entire study, all unit costs sequences can be charged.
- Also can be an efficient tool for long follow-up periods.
- The number of unit cost sequences should be limited.
Evaluation of a proposal with unit costs

- The proposal describes what is needed for the clinical study (resources, identical in each centre)

- Beneficiary/third party wishing to use the unit costs lists the costs of necessary resources, based on its closed accounts in year n-1

- The choice is neutral for the evaluation, there is no advantage in the evaluation for proposals with unit costs

- The technically/methodologically incorrect calculation will not have a negative impact on the evaluation. For successful proposal, the errors can either be corrected in the GAP stage or converted to actual costs.
## Unit costs - Calculation

<table>
<thead>
<tr>
<th>Task, Direct cost categories</th>
<th>Resource per patient/subject</th>
<th>Costs in year N-1</th>
<th>Costs in year N-1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Benef.(^a) 1</td>
<td>Benef.(^a) 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(short name)</td>
<td>(short name)</td>
</tr>
</tbody>
</table>

### Task No. 1

**Blood sample**

*(a) Personnel costs: - Doctors*

- **Other Medical Personnel**
  - Phlebotomy (nurse), 10 minutes
    - Costs in year N-1: 8,33 EUR\(^b\)
    - Costs in year N-1: 11,59 EUR\(^b\)

- **Technical Personnel**
  - Sample Processing (lab technician), 15 minutes
    - Costs in year N-1: 9,51 EUR\(^b\)
    - Costs in year N-1: 15,68 EUR\(^b\)

*(b) Costs of consumables:*

- Syringe
  - Costs in year N-1: XX EUR
  - Costs in year N-1: XX EUR

- Cannula
  - Costs in year N-1: XX EUR
  - Costs in year N-1: XX EUR

*(c) Costs of the medical equipment:*

- Blood container
  - Costs in year N-1: XX EUR
  - Costs in year N-1: XX EUR

- Use of -80° deep freezer, 60 days
  - Costs in year N-1: XX EUR
  - Costs in year N-1: XX EUR

- Use of centrifuge, 15 minutes
  - Costs in year N-1: XX EUR
  - Costs in year N-1: XX EUR

*(d) Services*

**Task No. X**

...  

...  

Total amount: 

- Costs in year N-1: XX EUR
- Costs in year N-1: XX EUR
Unit costs of **internally invoiced goods or services**

- Unit costs of goods or services internally invoiced and directly used for the action\(^1\)

- Examples: use of specific research devices or research facilities (MRI scanner, electron microscope, clean room), standard testing or research processes (genomic test, blood test), specialised premises for hosting a specimen used for the action (animal house)

- Unit costs per goods or services which the beneficiary itself produced or provided for the action

- *Calculation must be in line with the beneficiary’s **usual cost accounting practices** and applied in a **consistent manner**, regardless of the source of funding*

\(^1\) Article 6.2 D.5 MGA Version4

## Eligible costs – included into the price per unit calculation

<table>
<thead>
<tr>
<th>Description</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staff working for the MRI facility - physicists, radiology technical assistants, receptionist directly assigned to work for this specific imaging centre, radiologist reading the results</td>
<td></td>
</tr>
<tr>
<td>Consumables used for the MRI facility - e.g. contrast medium for imaging procedures, helium used for cooling</td>
<td></td>
</tr>
<tr>
<td>Depreciation of MRI scanner and other equipment directly linked to its use</td>
<td></td>
</tr>
<tr>
<td>Generic supplies like electricity and water – BUT only if the consumption of the MRI facility has been directly measured</td>
<td></td>
</tr>
<tr>
<td>Maintenance and service contracts for the MRI scanners – BUT only if the cost is directly identifiable - e.g. a separate invoice for the service contracts for the MRI scanner, not including other machinery of the hospital</td>
<td></td>
</tr>
<tr>
<td>Ineligible costs – not included in the calculation</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Cost of central services - e.g. accounting department, human resource department</td>
<td></td>
</tr>
<tr>
<td>Shared infrastructures - e.g. central heating, air-conditioning</td>
<td></td>
</tr>
<tr>
<td>Shared services - e.g. cleaning services, or central receptionist or appointment services</td>
<td></td>
</tr>
<tr>
<td>Depreciation of shared building - e.g. the MRI facility is part of the main building of the beneficiary</td>
<td></td>
</tr>
<tr>
<td>Costs already charged in other cost category or in other GA</td>
<td></td>
</tr>
<tr>
<td>If a cost is not used exclusively for the MRI facility, only a verifiable shared used for the MRI facility can be counted</td>
<td></td>
</tr>
<tr>
<td>Bank interests, provisions for future expenses and any other ineligible costs listed in Art. 6.5 H2020 MGA</td>
<td></td>
</tr>
</tbody>
</table>
Thank you!

@EUScienceInnov
#InvestEUresearch
#EUHealthResearch

http://ec.europa.eu/research/health
http://ec.europa.eu/research/participants/portal