Challenges in H2020 Clinical Trials

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Agenda

I. Template
'Essential information about clinical studies'

II. Mandatory deliverables

III. Status recruitment sites

IV. (Unit costs)

European Commission

Purpose

- Providing structured information to experts for evaluation
- Giving applicants the chance to provide detailed information about clinical studies without page limitations.
  Reasons: - Detailed but important information, e.g. about Scientific Advice Meetings, relevant (regulatory) guidelines, in- / exclusion- criteria, etc.
  - potentially high number of studies

- Providing necessary information to request 'unit costs' for CS

Available under 'call documents'[1] and in submission system

[1]Previous version: http://ec.europa.eu/research/participants/portal/doc/call/h2020/sc1-hco-01-2016/1677602-essential_information_for_clinical_studies_en.pdf

Template

Essential information about clinical studies

1.1 Identifier

1.2 Study design and endpoints

1.2.3 Relevant guidance documents

- The focus on **relevant (regulatory, e.g. EMA) guidelines** has been widened

1.3 Scientific advice / protocol assistance / communication with regulatory / competent authorities / ethics committees

- **Realistic!** planning to ensure receiving regulatory/ethics approvals **on time**!
- Availability of PIP?, or other requirements

1.4 Subjects/population(s)

1.5 Statistic analysis plan(ning) and power calculation

Template

Essential information about clinical studies

1.6 Cumulative safety and efficacy information

1.7 Conduct (1.7.1 key study milestones)

1.7.2 Description of recruitment strategy

- Detailed and **realistic!** planning of recruitment strategy:
  - ✓ Based on available evidence and data
  - ✓ Robust and coordinated with proposed contingency measures

1.7.6 Study medication

- **Binding agreements** and **realistic planning** to ensure:
  - ✓ On time availability of IMPD
  - ✓ Timely availability of study medication

1.8 Orphan designation

1.9 'Unit costs per patient' for clinical trials / studies / investigations

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Mandatory deliverables (1)

1) **'First study subject approvals package'**, for each included CS (prior to enrolment of first study subject):
   a. Final version of study protocol as submitted to regulators / ethics committee(s)
      (no need to change deliverable if later amendments)
   b. Registration number of the clinical study in a WHO- or ICMJE- approved registry
      (Please note: Result posting for the study must be possible)
   c. Approvals (ethics committees and national competent authority if applicable) required for the invitation / enrolment of the **first** subject in at least one clinical centre

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Mandatory deliverables (2)

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.

PLEASE NOTE

*"Extensions of project duration can generally **not** be granted in H2020. Significantly delayed key study milestones might lead to reduced EU contribution or the termination of the grant agreement."*

Mandatory deliverables (3)

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.

Status of
Recruitment sites

Clinical 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)

Status of
Recruitment sites

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 3rd party itself, not by the beneficiary!) when actual or unit costs are used

Status of
Recruitment sites

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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 in case of 100% reimbursement rate of direct costs, no more "shortfall" for linked beneficiary

Unit Costs

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Unit costs for clinical studies:

- have to be requested in the proposal
- have to be calculated according to the **defined methodology** of Commission Decision C(2016) 7553[1] (**based on historical costs of individual beneficiaries in last closed accounts**)
- use is voluntary for each beneficiary (no one-size-fits all for the consortium)
- combination of unit costs and actual costs are possible
- average personnel costs: pre-defined categories of doctors, other medical personnel, technical personnel

[1]http://ec.europa.eu/research/participants/data/ref/h2020/other/legal/unit_costs/unit_costs_clinical_studies.pdf

Detailed information

about

Unit costs & internal invoicing

Provided in the afternoon session

or under http://www.healthncp.net/news-events/webinar-clinical-studies-horizon2020-proposals

Thank you

www.ec.europa.eu/research/health

www.ec.europa.eu/research/horizon2020

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Applicability/Definition

1 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

Purpose

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Reasons:
- Detailed but important information, e.g. about Scientific Advice Meetings, relevant (regulatory) guidelines, in- / exclusion- criteria, etc.
- potentially high number of studies

- ❑ Providing necessary information to request 'unit costs'

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Scope

- Essential information – based on a generic CSP (Clinical Study Protocol)
- *When information is currently not available (e.g. a clinical study is planned for a later stage of the project and will be based on data of previous studies) the source of required data should be provided and / or the selection of the applied methodology should be described*
- *Each section must be shortly and concisely described. In case one or more issues do not apply to a particular study, please briefly explain/justify.*

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Applicability

- Use of template mandatory for certain single-stage and second-stage topics, **if** a clinical study is included
  - But: no eligibility criterion, no disadvantage when information provided in other part of proposal;
  - Rather: more and more appreciated (applicants, evaluators) as an opportunity for structured information
- These topics are listed in the template/Annex.

Applicability (2)

For stage I applications:

- Initiate timely planning of e.g.:
  - Recruitment strategy;
  - For requesting scientific advice / protocol assistance;
  - Study conduct, e.g. study medication
- Relevant key aspects of the template should be addressed also in stage I applications (even though the template itself cannot be up-loaded).

1.2.3 Relevant guidance documents

Relevant guidance documents, e.g. guidelines from:

- Scientific societies (e.g. addressing standard-of-care)
- Regulatory bodies – e.g. guidance notes from the European Medicines Agency – EMA, e.g.:
    - General and methodological 'Scientific guidelines'
        - 'ICH E9 Statistical principles for clinical trials'
        - 'Role of pharmacokinetics in the development of medicinal products in the paediatric population'
    - Disease specific 'Clinical efficacy and safety guidelines'
        - E.g. 'Clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus'
- HTA agencies

1.7.2 Description of recruitment strategy

Based on:

- Specification of criteria for site selection
- Estimation of expected (feasible+tested!) recruitment rates - based on main in-/exclusion criteria, main aspects of study conduct
- Contingency plans (e.g. inclusion of additional sites)

➢ Academic networks or research infrastructures, like ECRIN, may provide support by e.g.:

- Providing information on possible investigation centres
- Providing guidance documents or trainings
- Supporting feasibility assessment of recruitment planning via (national/regional) partners or specific networks.

Claimed costs ≠ reimbursed costs!

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Internal arrangements **for agreed reimbursement**
(independent of unit costs!)

Consortium **can** agree internally to *reimburse* **less** than the unit costs or **actual costs**!

- Example: (Unit) cost per subject vary between 1000 and 5000 EUR/subject for different beneficiaries, but consortium agrees on an reimbursement of 1000 EUR/subject for all beneficiaries.
- Practically the beneficiaries should claim the full/unit costs but request less (the agreed amount) as EU contribution
- The requested EU contribution cannot to be higher than the (unit or actual) costs!

Contract Research Organisations (CROs)

- Commercial CROs usually work 'for profit' and may not intend to join a consortium as beneficiary → In those cases the commission will consider accepting subcontracting
- Please note: It is not possible to reimburse CROs based on Article 10 MGA (Purchase of goods, works or services)
- **Academic CROs** exist (e.g. ECRIN network) – might be willing to become beneficiary!
- Only **limited part of the action** can be sub-contracted (Art. 13 MGA)

Subcontracting

Rule of thumb for subcontracting:

- If clinical study is the main activity of the project:
  - Core study expertise cannot be subcontracted, but certain parts (GMP manufacturing, monitoring etc.) might be subcontracted as long as general regulatory expertise is available and the study design, high-level study management and oversight remain as tasks within the consortium (budget share: not essential criterion!)
- If clinical study is just a small part of the project, i.e. most of the project is preclinical activity:
  - Study might be subcontracted in its entirety