#InvestEUresearch

# Horizon 2020 Work Programme for Research & Innovation 2018-2020

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

Cornelius Schmaltz, Head of Unit
Health Directorate
DG Research and Innovation
European Commission

Research and Innovation

# Clinical Studies

- **Why? What?**
- **Template – Essential information about clinical studies**
- **Do's and don'ts – key issues for evaluation**
- **Financial Issues: Clinical studies unit costs, Internal Invoicing**
- **Status of recruitment sites**
- **Deliverables**

# 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

- Adults
- Children
- Elderly
- Gender

- Phase I
- Phase II
- Phase III
- Observational studies

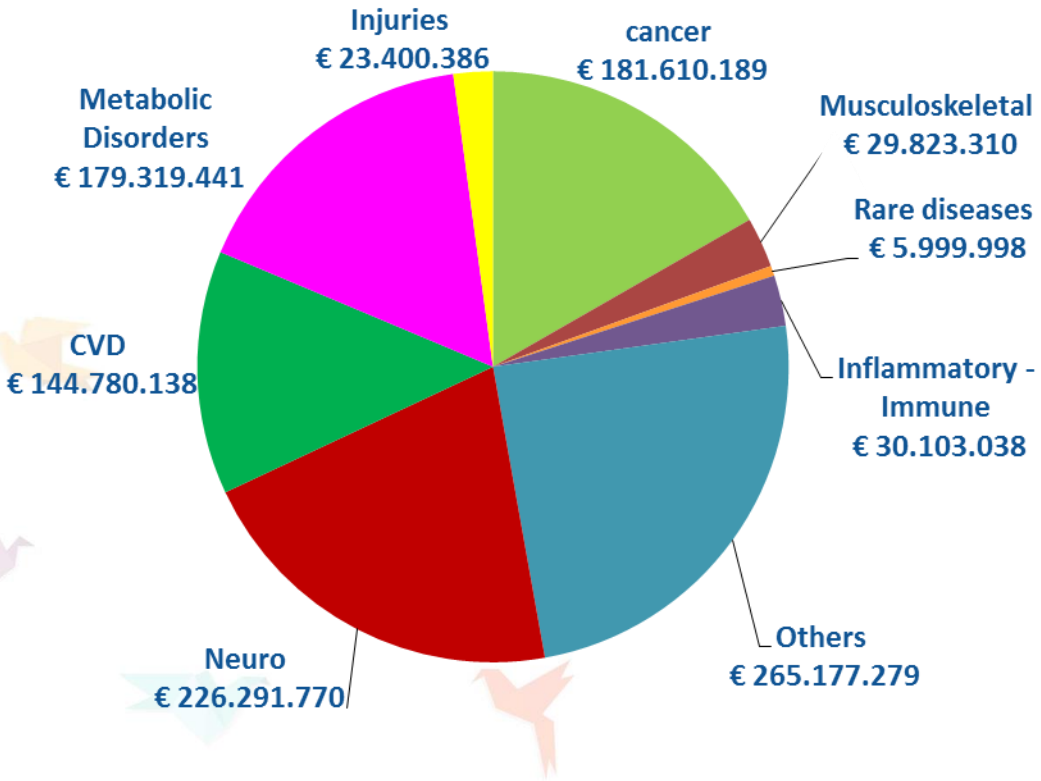
- Regenerative therapies
- Rare diseases
- Non-communicable diseases
- Infectious diseases
- Quality of life interventions
- Palliative care

- Off-patent trials
- Repurposing trials
- Paediatric trials
- Drug, surgery, radiotherapy, QoL trials
- Medical devices and companion diagnostics trials
- Comparative effectiveness trials

# Clinical Studies – What do we fund?

SEVENTH FRAMEWORK PROGRAMME

## > 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: around 50% of SC1 projects include clinical studies!**

European Commission

# 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[1] | PURPOSE APPLICABILITY

- 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 proposal
  - Rather: more and more appreciated (applicants, evaluators) as an **opportunity** for structured information

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

SCOPE

- Ethical considerations have to be addressed in the respective separate section
- 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."

# Template
# Essential information about clinical studies

UPDATES

## 1.2.2 Primary and secondary endpoint(s)

**Includes now:**

*Explain how patient priorities/preferences have been or will be taken into account in the proposed study (e.g in relation to selection of design, endpoints, study populations etc.).*

- This is not a request to provide letters of support.
- Patient priorities/preferences should be taken into account appropriately during and for the project planning and design of the clinical studies.
- A short but comprehensive summary of the strategy/approach should be included in this sub-section.

## Template
## Essential information about clinical studies

UPDATES

### 1.3 Regulatory status and activities

### 1.3.1 Regulatory / ethics status

**Request for specification included:** if the clinical study falls under Regulation EU No 536/2014 (Clinical Trials Regulation), Regulation EU No 2017/745 (Medical Devices) or Regulation EU No 2017/746 (In-Vitro Diagnostics).

### 1.3.2 Scientific advice / protocol assistance

**New sub-section,** request for concise, but comprehensive information about the planned activities

### 1.3.3 Qualification advice

**New sub-section,** request for concise, but comprehensive information about the planned activities

- Relevant e.g. for biomarker research

# Do's and don'ts – key issues for evaluation

- The **recruitment planning** has to be sufficiently detailed and realistic!
- **Contingency measures** have to be appropriate (ensuring that delays can be compensated) and realistic!
- If FIM / FIH (First in HuMan) application is intended in a clinical study, the descriptions of the '**FIM / FIH package**' (safety pharmacology / toxicology) has to be exhaustive, allowing experts to evaluate the risk of the project to (not) achieve the required ethics and regulatory approvals.
- If study medication is required sufficient information has to be provided allowing to evaluate if the planning is realistic.

# Clinical studies unit costs

- requested in the proposal (and evaluated)
- fixed methodology[1] (not beneficiary's own methodology!)
- *resources* (e.g. personnel time – identical for all beneficiaries) multiplied with *costs* (identified in the last closed accounts of each beneficiary)
- fixed for the entire duration of the project. No adjustments for inflation or wage increases during the time course of an action.
- can be combined with direct costs
- no need for time sheets and detailed actual costs for each patients
- only items that are audited: Number of patients enrolled and correctness of historical costs listed.
- more detailed explanations and calculation table in the template[2]



[1] Commission Decision C(2016) 7553 final (http://ec.europa.eu/research/participants/data/ref/h2020/other/legal/unit_costs/unit%20costs_clinical_studies.pdf)
[2] http://ec.europa.eu/research/participants/data/ref/h2020/other/legal/templ/h2020_tmpl-clinical-studies_2018-2020_en.pdf

# Unit costs of goods or services internally invoiced and directly used for the action[1]

- 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*
*http://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/amga/h2020-amga_en.pdf*

European Commission

# Internal invoicing - Example

| *Examples of costs **generally eligible** as part of the unit cost* | *Examples of costs **ineligible** as part of the unit cost* |
|---|---|
| – *staff working for the facility (e.g. keepers, veterinarians and other persons directly assigned to run the animal house)*<br>– *consumables used for the animal housing (e.g. animal food, bedding)*<br>– *depreciation of cages and other equipment directly linked to the housing of the animals*<br>– *generic supplies like electricity or water — BUT only if the consumption of the facility has been directly measured (so that the cost can be accurately determined)*<br>– *maintenance and cleaning of the animal house facility — BUT only if the cost is directly identifiable (e.g. a separate invoice for the cleaning of the cages)* | – *cost of central services (e.g. accounting department, human resources department)*<br>– *shared infrastructures (e.g. central heating, air-conditioning) and their maintenance*<br>– *shared services with no differentiation of the costs incurred for the animal house facility (e.g. cleaning services)*<br>– *depreciation of shared buildings (e.g. the animal housing is part of a main building of the beneficiary)*<br>– *bank interests, provisions for future expenses and any other ineligible costs listed in Article 6.5* |

# Status of recruitment sites (I)

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 (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

# 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

## Mandatory deliverables (I)

**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

## Mandatory deliverables (II)

**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.

Includes now:

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'

# Thank you!

@EUScienceInnov

**#InvestEUresearch**

**#EUHealthResearch**

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

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

European Commission