



The EU Framework Programme for Research and Innovation

**HORIZON 2020**

# **Clinical Studies in Horizon 2020**



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## I. Template

'Essential information about clinical studies'



## Financial and Contractual Aspects - Basics

- Clinical studies (CS) are subject to the same legal provisions and guidance notes as other activities in H2020 projects. No special 'derogations' (with the exception of special 'unit costs')
- BUT: Specific features of clinical studies require consistent application of existing rules



## Applicability/Definition

**1** A 'clinical study' is ... 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/subjects. It includes but is not limited to clinical trials in the sense of the EU Clinical Trials Directive (2001/20/EC).

- Broad, inclusive definition!

## Applicability

- Use of template mandatory for certain single-stage and second-stage topics
- These topics are listed in the template.
- **If**, a clinical study is included.

## Applicability

- ❑ For **each** clinical study<sup>1</sup> performed within the scope of the proposal ... compiled into one single document per proposal based on this template.
- ❑ In stage-1 proposals and in topics not listed, 'Essential information on clinical trials/studies/investigations' cannot be uploaded as a separate template. Instead, relevant aspects of this information must be integrated in part B of the proposal template. Nevertheless, the points listed below might serve as an orientation also in these cases.

## 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, in- / exclusion-criteria, etc.
- potentially high number of studies

- Providing necessary information to request 'unit costs'

Available under 'call documents'<sup>1</sup> and in submission system

<sup>1</sup>e.g.: [http://ec.europa.eu/research/participants/portal/doc/call/h2020/h2020-phc-2015-single-stage\\_rtd/1632634-essential\\_information\\_for\\_clinical\\_studies\\_2015callsv3\\_01122014\\_en.pdf](http://ec.europa.eu/research/participants/portal/doc/call/h2020/h2020-phc-2015-single-stage_rtd/1632634-essential_information_for_clinical_studies_2015callsv3_01122014_en.pdf)

### 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.*

## Scope

*Relevant information provided in this template does not need to be repeated elsewhere in the proposal, but can be referred to*

*Information provided that is not in the scope of this template will not be taken in account for the proposal evaluation.*

## Scope

- ❑ *Ethical considerations have to be addressed in the respective separate 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.***

**Please note: 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.**

## New version - main aspects (1)

### 1.2 Study design and endpoints

*1.2.3: Request for more detailed description of relevant guidance documents – scientific societies, competent authorities / EMA, HTA agencies*

### 1.7 Conduct

*1.7.1: Request for more detailed definition of key study milestones*

*1.7.2: Detailed description of the recruitment strategy*

## New version - main aspects (2)

**1.7.3:** *Definition of intervention assignment*

**1.7.4:** *Request for more detailed description of study / trial management, monitoring, data management etc.*

**1.7.5:** *Request for more detailed description of the role coordination centers and committees*

**Annex II:** *Mandatory deliverables for clinical studies now included in the template*

**P.S.:** *Don't forget to explain when special populations are excluded from the study*

### **Essential information** about clinical studies to be included in the **DoA**:

- All applicable sections of the template / each included study  
E.g. very important is scheduling for study conduct: Planning for first patient first visit, if applicable study medication etc.

The information has to be included in the DoA e.g. in section 2.3.1 as a task or a (part of) work package



# Questions



## II. Status 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)
- Subcontractor (Art. 13 MGA)
- Please note: It is not possible to reimburse recruitment sites based on Article 10 MGA.



## 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*



# Questions



## III. Subcontracting



## Subcontractor (Art. 13, MGA)

- *task (!) must be identified in DoA*
- *agreed 'price per patient/subject', profit possible*
- *best price/quality ratio, transparency 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***



## Research Organisations (CROs)

- Only **limited part of the action** can be subcontracted (Art. 13 MGA)
- **Academic CROs** exist (e.g. ECRIN network) – might be willing to become beneficiary!
- Commercial CROs usually work 'for profit' → Commission will consider accepting subcontracting
- Please note: It is not possible to reimburse CROs based on Article 10 MGA.



## CROs

### **Rule of thumb** for amount of 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



# Questions



## IV. Unit costs for clinical studies



## Based on Commission Decision C(2014) 1393<sup>1</sup>

### Unit costs are:

- a fixed reimbursement amount
  - for each study subject enrolled
  - in a given centre
  - calculated according to a defined methodology
  - based on historical costs of the **beneficiary/third party**
  - for the entire funding period of an action.
- [NOT a flexible tool, adjustments during the time course of an action are not possible.]

<sup>-1</sup> [http://ec.europa.eu/research/participants/data/ref/h2020/other/legal/unit\\_costs/unit%20costs\\_clinical\\_studies.pdf](http://ec.europa.eu/research/participants/data/ref/h2020/other/legal/unit_costs/unit%20costs_clinical_studies.pdf)



- ❑ **Unit costs can be used in any action under SC 1**
- ❑ **Unit costs** can be used by:
  - ❑ beneficiaries
  - ❑ linked third parties [Art. 14]
  - ❑ third parties contributing in kind to the clinical study [Art. 11]
- ❑ **Unit costs** can be used for any type of clinical study
- ❑ *Alternative to the use of actual costs, on **voluntary basis***

# Unit Costs

## Conditions I



- ❑ *Resources will be **evaluated with the proposal.***
  
- ❑ *Unit costs per patient/study subject fixed **for the entire duration** of the project.*
  
- ❑ ***Indirect costs** of the clinical study (25% of direct costs)*
  
- ❑ ***Excluded from unit costs:** Travel and subsistence costs of patients/subjects are not included (reimbursed on the basis of eligible costs actually incurred under the cost category “other direct costs”)*



- ❑ *Per clinical study **subject**: Estimation of the resources*
  - per task on the basis of the protocol,
  - the same for all beneficiaries involved.
  
- ❑ *Per **beneficiary**/third party: Calculation of costs based on historical costs*
  
- ❑ *Verification and **audit ex-post only**:*
  - number of patients/subjects declared = number of patients/subjects actually participating in the study
  - Beneficiary/third party has correctly identified the costs in its accounts of year n-1

# Unit Costs Calculation



Task, Direct cost categories	Resource per patient/subject	Costs in year N-1 Benef. <sup>a</sup> 1 (short name)	Costs in year N-1 Benef. <sup>a</sup> 2 (short name)
Task No. 1			
Blood sample			
(a) Personnel costs: - Doctors			
- Other Medical Personnel	Phlebotomy (nurse), 10 minutes	8,33 EUR <sup>b</sup>	11,59 EUR <sup>b</sup>
- Technical Personnel	Sample Processing (lab technician), 15 minutes	9,51 EUR <sup>b</sup>	15,68 EUR <sup>b</sup>
(b) Costs of consumables:	Syringe	XX EUR	XX EUR
	Cannula	XX EUR	XX EUR
	Blood container	XX EUR	XX EUR
(c) Costs of the medical equipment:	Use of -80° deep freezer, 60 days	XX EUR	XX EUR
....	Use of centrifuge, 15 minutes	XX EUR	XX EUR
(d) Services			
Task No. X			
...			
...			
<b>Total amount:</b>		<b>XX EUR</b>	<b>XX EUR</b>



## Unit cost component 'personnel costs' (1)

- **3 unique and exclusive (!) personnel categories:**
  - Doctors
  - Other medical personal
  - Technical personnel
  - No other personal category / calculation base for personal costs possible (e.g. categories for 'nurses' 'study nurses' or 'pharmacists' do not exist!)



## 'The magic 3 numbers'

**TIP**

*Ask your institution's accounting department for the average hourly rates calculated following the method explained in the Commission decision in year **N-1** for each of these three personnel categories: 'Doctors', 'Other medical personnel' and 'Technical personnel'!*

- Requesting these three rates once every year will cover personnel costs for any clinical study in your H2020 proposals for that year!
- Consider a similar approach for frequently used consumables or service contracts!



## Unit cost component 'personnel costs' (3)

*Average hourly cost for Doctors/ Other medical and Technical personnel*

**Average hourly cost =**

**Total personnel costs**

**1720 X FTE**

**Total personnel costs** = (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 or equivalent appointing act) for the **specific personnel category** (e.g. **all** doctors of a hospital) based on **historic costs** of year N-1 (certified or auditable documentation)

[see conditions set out in Article 6.1.A.1 of the model Horizon 2020 grant agreement]

**FTE** = number of full-time equivalent for the personnel category for year N-1

1720 = Working hours per year, **fixed rate**



### *Service contracts with external service providers – a way to integrate some laboratory costs*

- *Costs for the reimbursement of tasks carried out by external service providers, e.g. for certain laboratory analyses (but no internal invoicing) can be implemented in Unit Cost calculations under 'other specific service contracts'*
- *The costs for the same services (tasks) in the year N-1 have to be recorded in the accounts.*

# Unit Costs, combination with actual costs



- *In general the **combination** of different costs models is possible.*
- *The applicants can decide which method to use for which cost item.*
- *In some cases it can be most efficient to use the unit cost model only for the reimbursement of **personnel costs** while e.g. using the actual cost model for consumables.*
- *Also the combination with subcontracting is possible.*

# Unit Costs

## Serial unit costs



- *Unit costs can only be claimed for **patients that have completed** the entire protocol covered by the respective unit costs.*
- *When there are several treatment blocks, the establishment of sequential unit costs covering e.g. only one treatment sequence can be efficient. I.e. for a patient, who drops out after the first treatment block, only unit costs 1 can be charged. For patient who completes all three treatment blocks, unit costs 1, 2 and 3 can be charged.*
- *'Sequential unit costs' can also be an efficient tool for covering **long follow-up periods**.*

# Unit Costs Evaluation



- *The choice of the cost model for clinical trials is neutral for the evaluation, i.e. there is no advantage in the evaluation for proposals with unit costs or for proposals with actual costs.*
- *The technically/methodologically incorrect calculation/application of unit costs for clinical studies will not have a negative impact on the evaluation. If such proposals are successful, the errors in the calculation of unit costs can either be corrected or the costing method is converted to actual costs.*



## *Internal arrangements for agreed reimbursement*

□ If consortium agrees internally to reimburse less than the unit costs or actual costs, this is perfectly fine.

-**For example:** (Unit) cost per subject vary between 1000 and 5000 EUR/subject for different beneficiaries, but consortium agrees on an agreed 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) costs!



# Questions



## V. Mandatory deliverables



## 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 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 invitation / enrolment of **first** subject in at least one clinical centre



## Mandatory deliverables (2)

- 2) 'All approvals package'**, CS with more than 1 centre:  
*All* approvals from ethics committees and national competent authorities (if applicable) of all study sites once the last approval has been received.
  
- 3) '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 (3)

### 4) 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.



## Ethics approvals for CT (1)

- Note: Mandatory deliverables on approvals **are NOT sufficient for** compliance with Art. 34.2 of the MGA:
- *Before the beginning of an activity raising an ethical issue, the coordinator must submit to the [Commission] copy of:*
  - (a) any ethics committee opinion required under national law and
  - (b) any notification or authorisation for activities raising ethical issues required under national law.



## Ethics approvals for CT (2)

- *(cont'd:) If these documents are not in English, the coordinator must also submit an English summary of the submitted opinions, notifications and authorisations (containing, if available, the conclusions of the committee or authority concerned).*



# Questions

# Detailed information about

The template, Unit costs, Status recruitment sites,  
Subcontracting, Mandatory deliverables

- *Provided in the **back-up of this presentation***



**Thank you**

[www.ec.europa.eu/research/health](http://www.ec.europa.eu/research/health)

[www.ec.europa.eu/research/horizon2020](http://www.ec.europa.eu/research/horizon2020)



## Unit cost component 'personnel costs' (4)

- *Average hourly cost fictive example for Other medical personnel*

$$\text{Average hourly cost} = \frac{8\,596\,560}{1720 \times 100} = 49,98 \text{ €}$$

- ***Total personnel costs** for all 'other medical personnel' in the institution = (definition see above) = here 8 596 560 €*
- ***FTE** = (number of full-time equivalent for the personnel category for year N-1) = here 100*
- *1720 = Working hours per year, **fixed rate***
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## Unit cost component 'consumables' (2)

- *Average cost of the consumables (defined item or category)*

*Total costs of purchase of the consumables*

**Average cost of the consumables =** \_\_\_\_\_

*Total number of items (defined item or category) purchased in year N-1 of consumables concerned*



## Unit cost component 'consumables' (1)

- **Category of consumable:**
  - e.g. 10ml syringe type X of supplier Y
  - e.g. all types of 10 ml syringes in use in hospital Z in the year N-1
- **Total costs of purchase of the consumables** (defined item or category) = **Total value** of the supply contracts (including related duties, taxes and charges such as non-deductible VAT) **concluded by the beneficiary** for the consumables (defined item or category) delivered **in year N-1** provided (the supply contracts have to be compliant with H2020 rules, e.g. according to the principle of best value for money and without any conflict of interests).
  - [see conditions set out in Article 6.1.D.3 of the model Horizon 2020 grant agreement]
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## Unit cost component 'med. equipment' (1)

- **Category of medical equipment:**
  - A certain defined item (e.g. a deep freezer -20C type X of supplier Y)

**Total depreciation costs** = 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 or 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 (see conditions set out in Article 6.1.A.1 of the model Horizon 2020 grant agreement)



## Unit cost component 'med. equipment' (2)

**Total costs of purchase of services** = Total value of the contracts concluded by the beneficiary (including related duties, taxes and charges such as non-deductible VAT) for services delivered in year N-1 for the functioning of the equipment, provided the contracts were awarded according to the principle of best value for money and without any conflict of interests (see conditions set out in Article 6.1.D.3 of the model Horizon 2020 grant agreement)

**Total capacity** = Total time of use of the equipment expressed in hours, days or months and supported by evidence or the number of accesses to the equipment, for which supporting evidence may take the form of records or electronic log of units-of-access provision. The total capacity must take due account of real constraints (e.g. opening hours), but must reflect the equipment full capacity and include any time.

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## Unit cost component 'med. equipment' (3)

- *Average cost of medical equipment* *(defined item)*

$$\text{Average cost of medical equipment} = \frac{\text{Total depreciation costs} + \text{Total costs of purchase of services}}{\text{Total capacity}}$$



## 'other specific service contracts' (2)

- **Total costs of purchase of a service** = 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
- (see conditions set out in Article 6.1.D.3 of the model Horizon 2020 grant agreement)

**Total costs of purchase of the service**

**Average cost of a specific service per patient or subject** =

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*Total number of patients or subjects included in the clinical studies for which the specific service was delivered in year N-1*