Fit for Health 2.0

Support to SMEs & Researchers in FP7 and Horizon 2020 health-oriented projects

Clinical Trials in Horizon 2020

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Workshop
"Point of Care Device Commercialisation"

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What is a 'clinical trial' in H2020?

A 'clinical study' is defined for the purpose [of this template] 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.

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

Content

1. **Proposal preparation**:
    a) Planning:
        1. Composition of the consortium
        2. Budget issues
        3. Time planning
    b) Writing
        1. Description of the trial
        2. Ethics (section 5.1 and annexes)
2. **Implementation**:
    a) Management
    b) Monitoring

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Consortium

Composition of the consortium

- Experienced partners needed! Clinical trials (CT) are always a challenge;
  - → H2020 has been adapted to better accommodate the implementation of CT, but is not primarily designed for CT

- 2 different approaches:
  - make trial visible and living part of the project, full inclusion
  - Trial as data source, outsource in (large) parts

- Recruiting centers : different options to be involved
- Inclusion of a Contract Research Organisation (CRO)

Consortium

How to involve a study site?

Study site included as	Pro's	Con's
Partner (Beneficiary)	Preferred option for the EC Clear rules Overhead Visibility	Large consortium Inflexible (e.g. recruitment, selection of sites)
Subcontractor	Small consortium High flexibility Simple Administration Profit possible	Not applicable for core tasks Procurement rules to be applied „best value for money" No Overhead for beneficiary
In-kind contribution (patient data) provided by third parties against payment	Small consortium Overhead can be claimed by 3rd party	Must be identified in DoA → inflexible No profit High documentation load (cost documentation as for beneficiaries)
Affiliated entities and third parties with a legal link to a beneficiary	Small consortium Overhead can be claimed by 3rd party	Definition „legal link" leaves room for interpretation

Consortium

Inclusion of Contract Research Organizations (CROs)

- CT is the main activity of the project → Core CT expertise (e.g. study design, general regulatory expertise,) needs to be available in consortium

  BUT: subcontracting of specialized services e.g. for PK, professional trial monitoring etc. from CROs possible
- **'Academic CROs' exist** (e.g. ECRIN network) – might be willing to become a beneficiary; in that case: full partners, i.e. involved from the planning phase on and active partners in study design (alternatively: provide guidance/support as part of an advisory board?)
- Inclusion of a **commercial CROs** as beneficiaries also possible but commercial CROs usually work 'for profit' → might not be willing to become a beneficiary
  → in these cases, subcontracting could be an option

  BUT: In most cases, only limited part of the action can be subcontracted

Budget

- Clinical studies 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'**
- Use of unit costs is voluntary
- Beneficiaries can use different forms of reimbursement (unit costs or actual costs) for different clinical studies
- Unit costs have to be requested in the proposal → detailed and complete calculation must be provided with the "Template for essential information…"

Budget

Unit Costs

Based on Commission Decision C(2014) 1393 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

MUST READ!

Budget

Unit Costs

Advantages

- Ex-ante acceptance of unit costs = No need for time sheets and detailed tracking of resources used!

- Unit costs should encourage consortia to more realistically estimate their budget and time management for clinical studies.

Disadvantage

- NOT a flexible tool, adjustments during the time course of an action are not possible

Time planning

Don‘t be over ambitious!

Experience has shown that almost 50% of all FP7 projects were not finished in the originally planned time. Proper time planning is even more challenging for clinical trials activities:

- Project start date ≠ start of the study… esp. if **ethical approval** still needs to be obtained
- Time for **protocol development** (proposal includes draft protocol only.. development of final protocol may take some time, esp. if part of the work plan)
- **Slow recruitment**

’No’ flexibility regarding duration – Project extensions can generally not be granted in H2020.

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Description of the trial

Where in the proposal do I describe my study, and what's the appropriate amount of detail?

- **"Template for essential information to be provided for proposals including clinical trials"**… where mandatory
  - in standardized format, in great detail, one description per study
  - Always download latest new clinical trial template!

- **Proposal body**... in condensed format, summarizing the essence
  - with cross references to the study template / Annex

Proposal body - structure

1. Excellence
   - 1.1 Objectives
   - 1.2 Relation to the work programme
   - 1.3 Concept and methodology
   - 1.4 Ambition
2. Impact
   - 2.1 Expected impacts
   - 2.2 Measures to maximise impact
     - Dissemination and exploitation of results
     - Communication activities
3. Implementation
   - 3.1 Work plan - Work packages, deliverables
   - 3.2 Management structure, milestones and procedures
   - 3.3 Consortium as a whole
   - 3.4 Resources to be committed
4. Members of the consortium
   - 4.1. Participants (applicants)
   - 4.2. Third parties involved in the project (including use of third party resources)
5. Ethics and Security
   - 5.1 Ethics
   - 5.2 Security

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3 mandatory Ds!

Mandatory deliverables for H2020 clinical trials

1. **'First study subject approvals package'**,
   a. Final version of the study protocol
   b. Registration number of clinical study
   c. Regulatory and/or ethics approvals

2. **'Midterm recruitment report'**
   to be scheduled for the time point when 50% of the study population is expected to have been recruited

3. **'Report on status of posting results' in the study registry(s)**

Description of the trial: Template

Clinical study No.1

- 1.1 Identifier
- 1.2 Study design and endpoints
- 1.3 Scientific advice / protocol assistance / communication with regulatory / competent authorities / ethics committees
- 1.4 Subjects/population(s)
- 1.5 Statistic analysis and power calculation
- 1.6 Cumulative safety and efficacy information
- 1.7 Conduct
- 1.8 Orphan designation
- 1.9 'Unit costs per patient' for clinical trials / studies / investigations

If no beneficiary intends to use unit costs, the unit costs section does not need to be completed!

Clinical study No.2

- 2.1 Identifier
- …

In case one or more issues do not apply to a particular study, please briefly explain/justify

Ethics

Where in the proposal do I deal with ethical aspects of my planned work, and what‘s the appropriate degree of detail?

- Ethics issues table
- Proposal section 5.1
- “Supporting documents” (as annex)

Ethics

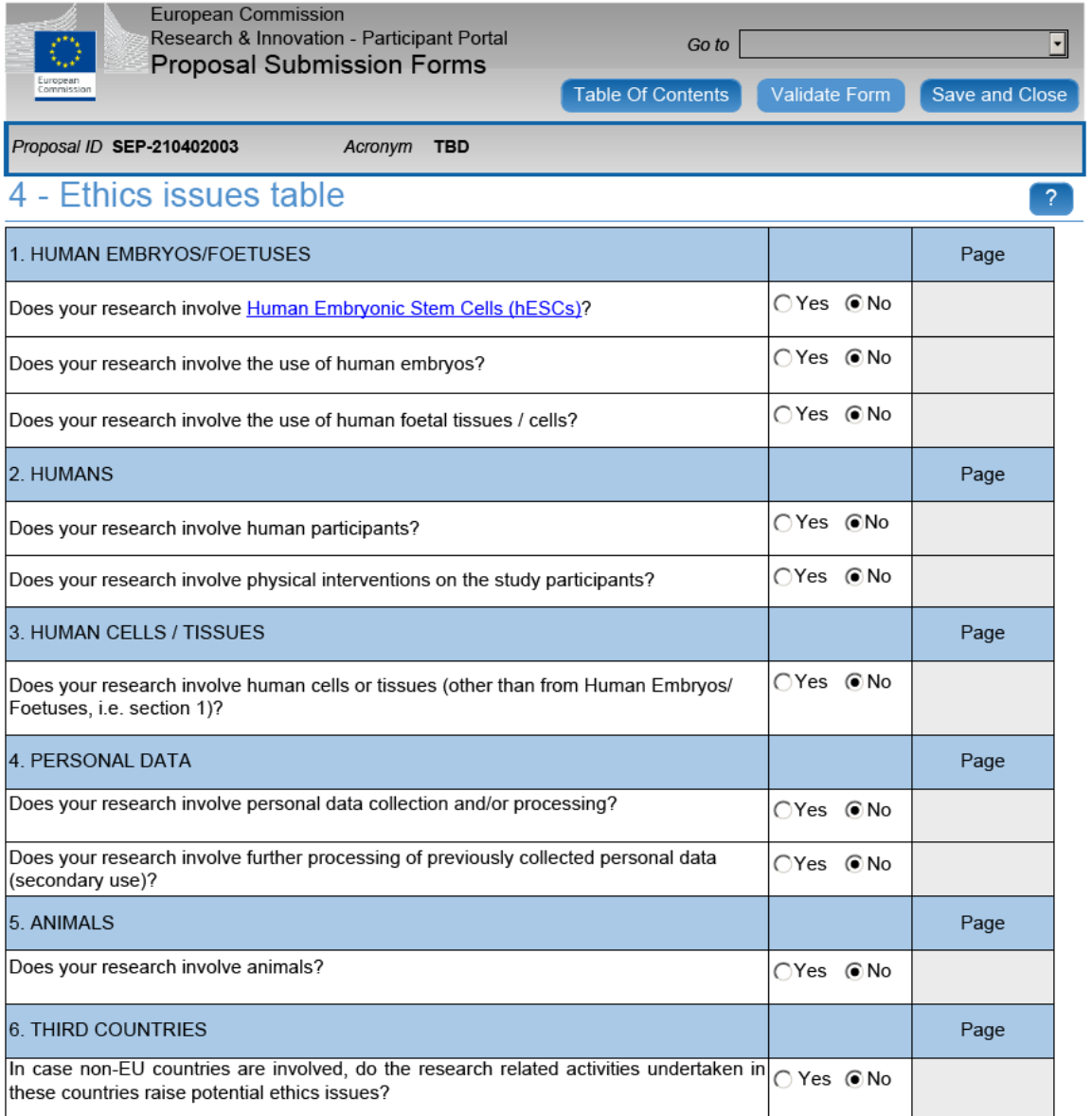
Ethics issues table online:

- collect from all partners

- have coordinator check / complete

THEN

optimally:
have one designated person in charge of all ethics aspects in your proposal
(…and project)



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Proposal ID **SEP-210402003** *Acronym* **TBD**

4 - Ethics issues table

1. HUMAN EMBRYOS/FOETUSES		Page
Does your research involve Human Embryonic Stem Cells (hESCs)?	○ Yes ◉ No	
Does your research involve the use of human embryos?	○ Yes ◉ No	
Does your research involve the use of human foetal tissues / cells?	○ Yes ◉ No	
2. HUMANS		**Page**
Does your research involve human participants?	○ Yes ◉ No	
Does your research involve physical interventions on the study participants?	○ Yes ◉ No	
3. HUMAN CELLS / TISSUES		**Page**
Does your research involve human cells or tissues (other than from Human Embryos/ Foetuses, i.e. section 1)?	○ Yes ◉ No	
4. PERSONAL DATA		**Page**
Does your research involve personal data collection and/or processing?	○ Yes ◉ No	
Does your research involve further processing of previously collected personal data (secondary use)?	○ Yes ◉ No	
5. ANIMALS		**Page**
Does your research involve animals?	○ Yes ◉ No	
6. THIRD COUNTRIES		**Page**
In case non-EU countries are involved, do the research related activities undertaken in these countries raise potential ethics issues?	○ Yes ◉ No	

Ethics

EC Guide "How to complete your ethics self-assessment"

For each item in checklist:

- **Info** to be provided **in section 5.1**
- **Documentation** to be provided in Annex **"supporting documents"**

Section 2: HUMANS		YES/ NO		Page	Information to be provided	Documents to be provided/kept on file
Does your research involve human participants?		☐	☐		Confirm that informed consent has been obtained. **plus:**	Informed Consent Forms + Information Sheets. **plus:**
If	- Are they social or human sciences research?	☐	☐		Details of recruitment, inclusion and exclusion criteria and informed consent procedures.	Copies of ethics approvals (if required).
	- Are they persons unable to give informed consent children/minors)?	☐	☐		Details of your procedures for obtaining approval from the guardian/ legal agreement of the children o other minors. What steps will you take to ensure that participants are not subjected to any form of coercion?	Copies of ethics approvals.
	- Are they vulnerable individuals or groups?	☐	☐		Details of the type of vulnerability. Details of recruitment, inclusion and exclusion criteria and informed consent procedures. These must demonstrate appropriate efforts to ensur fully informed understanding of the implications of participation	Copies of ethics approvals.
	- Are they	☐	☐		Details of the age range.	Copies of ethics

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Management

- CT is like a project within your project, with its specific set of actions, large number of individuals involved, need for harmonization, communication, coordination… → to be managed by a **highly experienced (clinical) partner or CRO**

- to be complemented by the **management of (and guidance for) ethical issues** → by an ethics expert (committee), and

- to be integrated into the H2020 project and regulatory framework → management of interfaces and H2020 project itself by a **classical project manager**

Management issues: working with patients

Patient availability / recruitment delays

- Estimates based on thorough feasibility analyses
- Common challenges: higher drop-outs than expected, new competing studies, changes in legislation, changes related to personnel conducting the work..
- Upcoming challenges MUST be reported quickly and fully

Management

- must **establish a trustful and close relationship with each site**
- must **know and optimize workflows**, and reduce admin challenges to a minimum
- should be ready and able to react promptly
- should ensure a **close monitoring** of recruitment numbers at all sites
- must have **strategies in place** to compensate for lower than expected patient numbers, reaching the original targets in the original timeframe with the fixed budget

Monitoring

- Official reporting in H2020: every 18 months,
  with the possibility of additional monitoring activities as the coordinator/management team sees fit to optimize implementation (e.g. interim reports)

Additional specific requirements for monitoring/reporting CT:

- three mandatory deliverables (EC)

- closer monitoring and much more (basic) reporting back of information is definitely needed (e.g. monthly reporting of recruitment numbers, monthly TCs with all clinical partners, etc.)

Concluding remarks

- Introduced during FP7, clinical trials implementation is rather new to EU Framework Programmes
- In H2020, CT are a central issue in Health calls (SC1); the EC has made great efforts to accommodate the needs of consortia willing to implement clinical studies
- H2020 provides challenges but also great opportunities for the implementation of clinical trials
- Be careful but don't be scared

Info and support

Sources of advice and support:

- National Contact Points
- FAQs concerning the H2020 societal challenge “Health, demographic change and wellbeing” https://ec.europa.eu/research/participants/portal/doc/call/h2020/sc1-pm-03-2017/1730125-faqs_v5_august2016_en.pdf
- Commission Decision C(2014) 1393
- EU IPR helpdesk: www.iprhelpdesk.eu
- FFH 2.0 CT factsheet
- FFH 2.0 support

Thank you!

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