Fit for Health 2.0

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

Clinical Trials in Horizon 2020

www.fitforhealth.eu

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Dr. Claudia Schacht | Eurice GmbH

What is a ‘clinical trial’ in H2020?

Or more specifically: What needs to be described as a ‚clinical study‘ in the proposal?

- *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).*

- A clinical study can be the core of a project, or part of a project
- …included in a project designed in response to a topic that specifically asks for a clinical study, or not
- i.e. highly relevant issue for anyone who is considering a proposal submission under SC1

Content

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

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Consortium

Composition of the consortium

- Experienced partners needed! Clinical trials are always a challenge; in H2020 even more so
- H2020 has been adapted to better accommodate the implementation of CT, but is not primarily designed for CT →
  - Different budgeting approach
  - 'No' flexibility regarding duration
  - Unexperienced partners often find EU FP participation a challenge in itself…
- 2 different approaches:
  - make trial visible and living part of the project, full inclusion, EU FP capacity building, investment in one project will pay off in later/other project
  - Trial as data source, outsource in (large) parts
- Recruiting centers as beneficiaries vs subcontractors
- Inclusion of a CRO

Consortium

Inclusion of Contract Research Organizations (CROs)

- Core CT expertise needs to be available in consortium
- BUT: specialized services e.g. for PK, regulatory support, professional trial monitoring etc. from CROs might be needed / ensure professional support and smooth CT implementation (NOT replacing any of the usual project management needs and structures; CT specific)
- 'Academic CROs' exist (e.g. ECRIN network) – involvement as a beneficiary suggested by the EC (alternatively: provide guidance/support as part of an advisory board?)
- Inclusion of 'regular' CROs as beneficiaries also possible (in that case: full partners, i.e. involved from the planning phase on and active partners in study design)
- Some CROs that work on a 'for profit' basis 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

CT are even more prone to under-budgeting than ‚regular' H2020 projects

- Careful to include all needs
- EU FP budgeting is done by adding up of individual components, not by giving a (well informed, many times confirmed) overall total as profit margins are not allowed
- Equally challenging (if not 'as impossible') as a comprehensive list of all activities in one day... hardly ever complete
- Additional challenges: e.g. plan for adaptation of (number of) recruiting centers, deal with drop-outs, avoid by all means slow-down of activities due to cashflow issues
- Unit costs vs actual costs, tbd

Budget

Unit Costs

- Use of unit costs is an alternative to the use of actual costs
- Use is voluntary, i.e. each beneficiary can decide whether to be reimbursed on the basis of unit costs or actual costs for a given clinical study
- Beneficiaries can use different forms of reimbursement (unit costs or actual costs) for different clinical studies
- Costs that are covered by unit costs cannot be declared as actual costs
- When a beneficiary intends to use unit costs, a detailed and complete calculation must be provided with the "Template for essential information to be provided for proposals including clinical trials"

Budget

Unit Costs

- Direct costs must be determined by estimating the resources used per task and per patient or subject and using its historical costs for these resources
- Beneficiaries must estimate the resources used specifically per patient for the conduct of the clinical study (e.g. personnel costs of doctors, other medical personnel and technical personnel; costs of medical equipment and costs of other service contracts) on the basis of the protocol for the clinical study
- Resource estimate must be the same for all members of the consortium using unit costs in a particular study
- Beneficiaries must use as historical costs the costs recorded in their certified or auditable profit and loss account for year N-1 (last closed financial year at the time of submission of the grant application)
- Amount of unit costs per patient is fixed in the grant agreement for the entire duration of the project, without adjustment for inflation

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 of a challenge for clinical trials activities:

- Project start date ≠ start of the study… esp if ethical approval still needs to be obtained (which is usually the case if a new/additional approval is needed for work under the project)
- Time for protocol development (proposal includes draft protocol only.. development of final protocol may take some time, esp if initiated after start of the project as part of the workplan)
- Slow recruitment
- Stage 1 planning often more ambitious, stage 2 planning more specific/sometimes longer duration advisable (all significant changes need to be justified)

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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 (currently: for all clinical studies included in a single-stage- or stage-2 proposal submitted to topics PHC-2, PHC-3, PHC-11, PHC-14, PHC-15, PHC-16, PHC-18, PHC-22, PHC-24, PHC-33 and HCO-6)
  - in standardized format, in great detail, one description per study
  - new clinical trial template for download

- Proposal body... in any case
  - in condensed format, summarizing the essence
  - as part of the overall description of the planned work, and
  - in parts in the WP description
  - with cross references to the study template / Annex

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
- 1.6 Cumulative safety information
- 1.7 Conduct
- 1.8 Orphan
- 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
- …

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"

Ethics

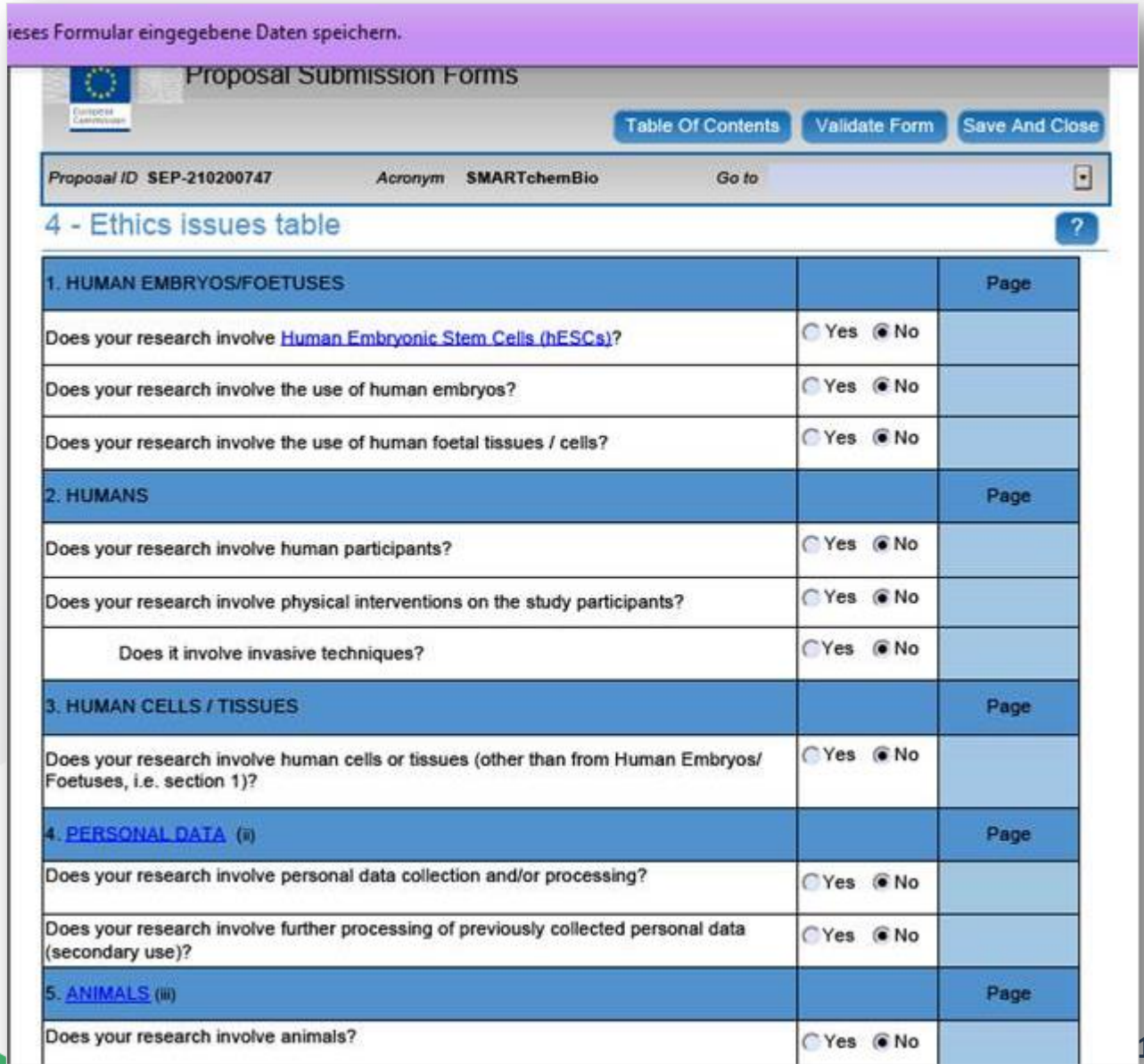
Ethics issues table online:

- 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)



ieses Formular eingegebene Daten speichern.

Proposal Submission Forms

Table Of Contents | Validate Form | Save And Close

Proposal ID **SEP-210200747** *Acronym* **SMARTchemBio** *Go to*

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	
Does it involve invasive techniques?	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 (ii)		**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 (iii)		**Page**
Does your research involve animals?	Yes No	

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Ethics

Proposal section 5.1:

In section 5.1

In sub-sections of section 5.1 (one for each issue ticked… see guide)

In Annex „supporting docs“

5.1 Ethics

If you have entered any ethics issues in the ethical issue table in the administrative proposal forms, you must:

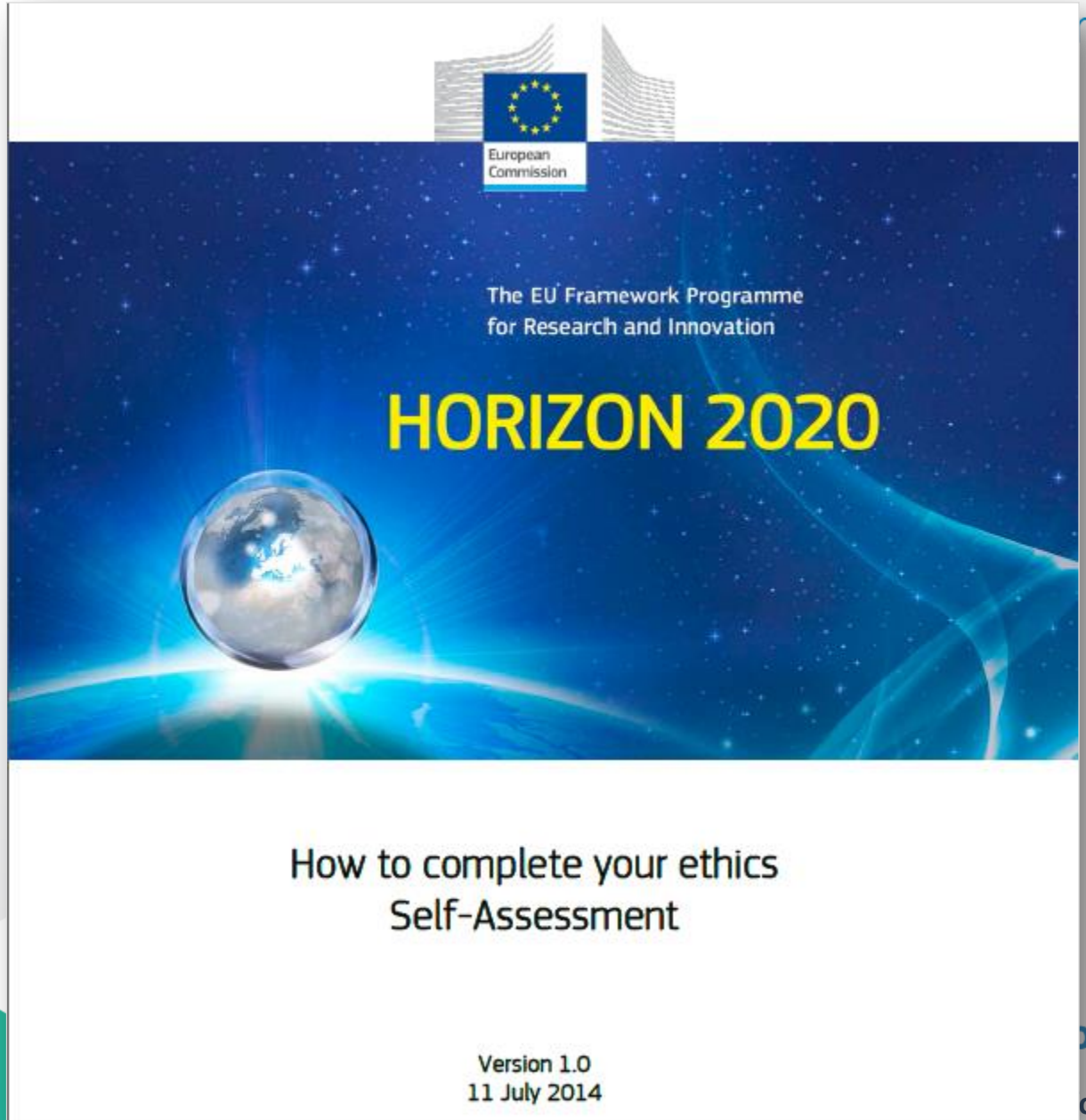
- submit an ethics self-assessment, which:
  - describes how the proposal meets the national legal and ethical requirements of the country or countries where the tasks raising ethical issues are to be carried out;
  - explains in detail how you intend to address the issues in the ethical issues table, in particular as regard:
    - research objectives (e.g. study of vulnerable populations, dual use, etc.)
    - research methodology (e.g. clinical trials, involvement of children and related consent procedures, protection of any data collected, etc.)
    - the potential impact of the research (e.g. dual use issues, environmental damage, stigmatisation of particular social groups, political or financial retaliation, benefit-sharing, malevolent use , etc.).
- provide the documents that you need under national law(if you already have them), e.g.:
  - an ethics committee opinion;
  - the document notifying activities raising ethical issues or authorising such activities

⚠ *If these documents are not in English, you must also submit an English summary of them (containing, if available, the conclusions of the committee or authority concerned).*

⚠ *If you plan to request these documents specifically for the project you are proposing, your request must contain an explicit reference to the project title.*

Ethics

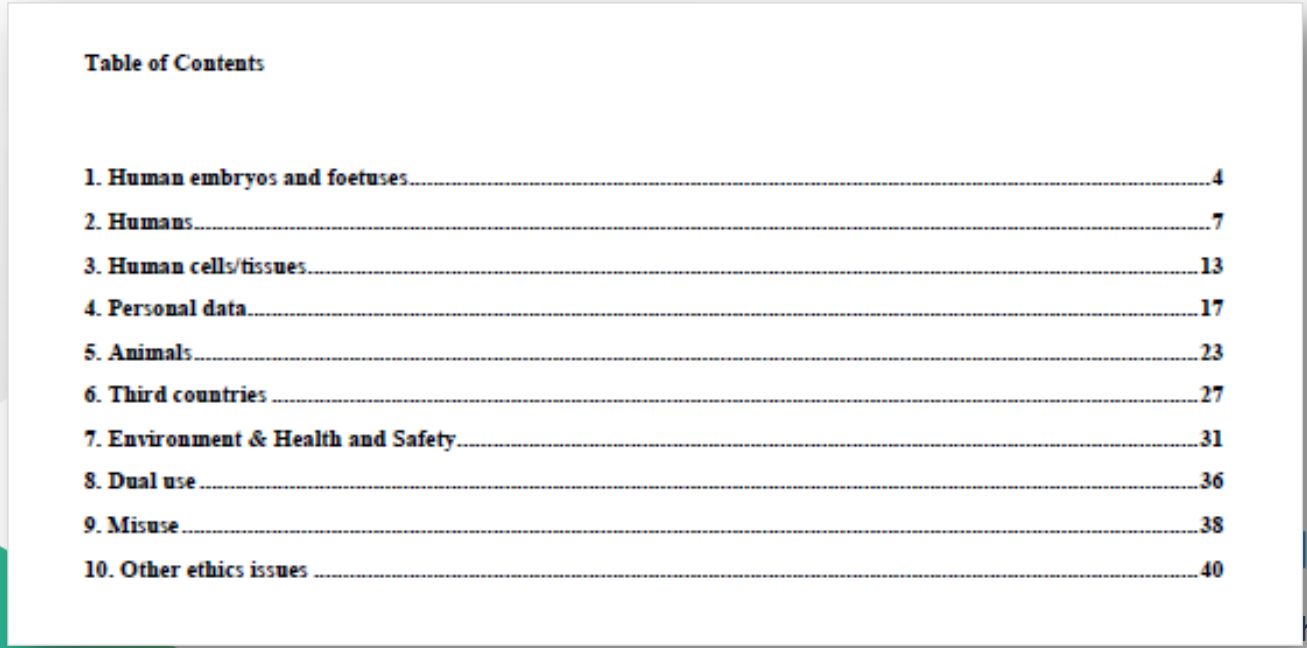
EC guide:



Ethics

„How to complete your ethics self assessment“

- Very helpful ‘how to’ guide
- Detailed step-by-step advice on how to deal with classic cases (what to describe, how to describe, what documentation to add)
- Ethics issues that are not covered must be dealt with outside the guide!



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9. Misuse 38
10. Other ethics issues 40

Ethics

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
Does your research involve human participants?		☐	☐		Confirm that informed consent has been obtained. plus:	Informed Consent Forms + Information Sheets (see text box below). plus:
If YES:	- Are they volunteers for social or human sciences research?	☐	☐		Details on recruitment, inclusion and exclusion criteria and informed	Copies of Ethics Approvals (if required).
	- Are they persons unable to give informed consent (including children/minors)?	☐	☐		Details on your procedures to obtain approval from guardian/ legal representative. Details on the measures you intend to take to ensure that there is no coercion on participants.	Copies of Ethics Approvals.
	- Are they vulnerable individuals or groups?	☐	☐		Details on the type of vulnerability. Details on recruitment, inclusion and	Copies of Ethics Approvals.

Changes between stage 1 and stage 2

Need to be explicitly addressed:

6. **Preparation of a stage 2 proposal**

If I am successful at stage 1, can I make changes to my proposal when submitting the full version to stage 2?

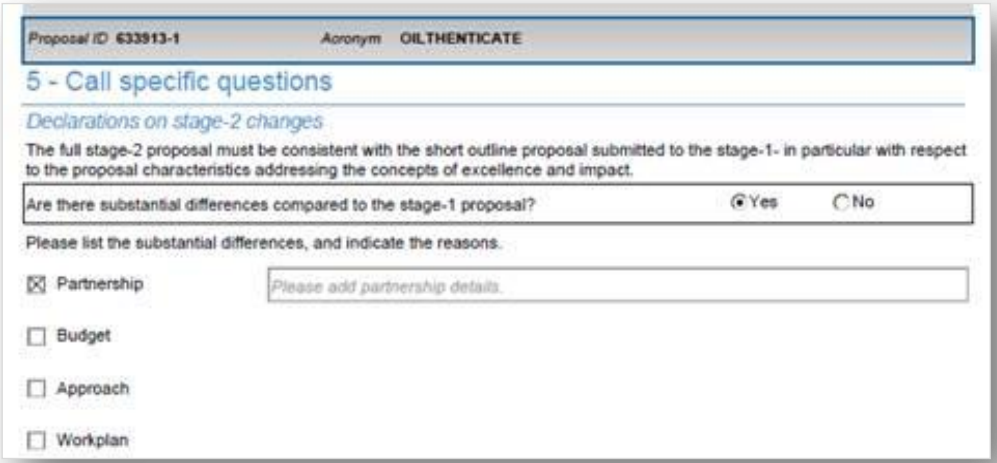
Section III.5.2 of the Horizon 2020 Grants manual: Section on: proposal submission and evaluation states that for two-stage submission schemes, 'the full proposal must be consistent with the short outline proposal and may not differ substantially'.

This means that changes are not recommended, but if absolutely necessary, they should be clearly explained and the evaluators will determine whether or not these changes are legitimate, and whether or not their insertion compromises the evaluator judgement made at stage 1.

Changes between stage 1 and stage 2

Need to be explicitly addressed

- For some SCs it was possible to address 'Call specific questions (Declarations on stage-2 changes)' in ECAS - this was NOT possible for SC1 (H2020-PHC-2014 topics)



- Instead:
  - highlight at the very beginning of your proposal body, or
  - highlight in the proposal section where it the issue is mentioned (e.g. consortium: on cover page; duration: where mentioned, and as a comment on Pert..)

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Management

Management of a clinical trial is not just an add-on to classical project management

AND

vice versa: the management of your project is not taken care of if including a CRO to look after your trial

- 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

Monitoring

The CT is to be implemented under H2020, but comes with additional requirements

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

The same basically applies to clinical trials:

- While specific requirements for CT elements in H2020 proposals, no specific EC requirements for monitoring/reporting
  BUT
- 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

- Clinical trials implementation is rather new to EU Framework Programmes
- Introduced during FP7
- In H2020, CT are a central issue in 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” http://ec.europa.eu/research/participants/portal/doc/call/h2020/h2020-hco-2015/1637625-2015_01_15_sc1_h2020_faq_en.pdf
- EU IPR helpdesk: www.iprhelpdesk.eu
- FFH 2.0 CT factsheet
- FFH 2.0 support

Thank you!

Dr. Claudia Schacht| Eurice GmbH

c.schacht@eurice.eu | www.eurice.eu