FAQs

Webinar: Clinical Trial 9.9.2014

Table of content

01_Template

How/where do you use the protocol in the H2020 application? There is a specific appendix in H2020 about the essential information on clinical trials. How does this relate to the protocol?

Some of the information that is part of the protocol will also appear in the proposal body at places where you describe your study. The protocol as such can be included in a draft version as part of the extra documents that are to be uploaded. The final protocol does not have to be part of the proposal.

Is the compulsory annex also used for the evaluation, e.g.: we do not have to repeat what we said, to cut down the number of pages? What level of information is expected at stage 1?

Annexes are to be uploaded with the full proposal, and yes, accessible for the evaluators. You do not have to repeat everything in the proposal body, but can be more concise there and make cross references to the annexes. In stage 1, you must be very brief, as the overall page limit is the same for all proposals, including those that entail clinical study elements.

If the template is not mandatory, can we anyway use it as an annex, to 'save' place in the proposal?

The template can only be uploaded for those topics that are marked accordingly. For all other topics, you can use it as a 'checklist' to make sure you cover all relevant aspects, but cannot upload it. All info needs to be mentioned in the proposal body in those cases.

You have pointed out PHC11 as a call requesting for clinical trials and indicated with an asterisk. This is not the case in the work program. Can you please clarify whether the clinical trial approach is mandatory?

In the version of August 2014 it is mentioned: " Single-stage- and stage-2 proposals: The use of this template is mandatory 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-62. For these topics, you will have the possibility to upload the completed template as a separate part of your application in the submission system."

For a recent PHC-2014 call I have uploaded the clinical trial template even while it was not required for the topic. Might be that this is no longer possible for the 2015 topics?

Yes, this was a technical mistake.

Must the template for clinical studies be uploaded together with Part B (included) or as separate PDF in the PPT?

As a separate document.

02 (Unit) Costs / Budget

Remark: you may use different approaches (unit costs/actual costs) for one beneficiary for different clinical trials.

Yes, this is true. Unit costs per patients have to be used for ALL patients of a beneficiary, for ONE CT. For a second CT, a second template will be filled-in (make sure to upload in ONE document).

Unit costs "for all patients at this institution": If one institution participates in several proposals: Must unit costs be used for ALL proposal or is this just "all patients within this project"?

The use of unit costs is a decision that can be made project by project, i.e. one institution can use unit costs in one project and actual costs in another project.

Can unit costs be used for linked third parties even if the beneficiary they are linked to does not use them?

Yes - they would have to be defined for that linked third party specifically in any case.

If the project involves more partners from different countries, how can we define the unit cost per patient, considering that each country may have different costs?

Unit costs are partner specific - i.e. you will most likely have different unit costs for each partner.

What about hospital admittance costs?

Any costs that will be reimbursed by health care providers/ insurance are NOT eligible for funding via the EU project.

For the Certificate on Financial Statement and an audit by the EC, I assume that the beneficiary should be able to specify the unit costs with actual and auditable costs (which origin from the year in which the application was written)? In other words, it cannot be a ballpark figure?

No ballpark figure, no. Numbers must be based on actual costs recorded in last closed accounts of beneficiary, described in detail in the full proposal, and will be assessed by the evaluators.

Can costs for the experimental drugs be regarded as consumables?

Study medication I personally would put under "other direct costs", but NOT to use in the "unit costs per patient". With the study medication, you have some more steps to get funded: packaging, blinding/ coding, maybe even (GMP) manufacturing. Overall, I would put it as bigger tasks than just as "consumables".

In the scope of PHC14: as the clinical development is depending on the data that will be obtained in preclinical studies, it will be difficult to have a precise budget to submit. How detailed should be the submitted budget in such a case? How detailed must be the study information that we will submit to H2020?

For PHC 14 (rare diseases) you are advised to contact EMA very early in the process. This is: before submitting stage 2 you MUST HAVE received orphan drug designation, so start contacting EMA today!
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp&mid=WC0b01ac05800240ce;
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp&mid=WC0b01ac05800240ce

How are the unit costs audited and on what extent the details must be identifiable in the accounts of the beneficiary? In other words, can we include in the unit costs that are usually used by hospitals, based on a national tariff system?

Unit costs that are usually used by hospitals may be a very good option for estimates on some components of your unit costs per patient, yes. Please note that costs which are paid for by the national health system cannot be charged to the project though. The calculation of the unit costs (see table in template for clinical studies) will become part of the Grant Agreement (Annex II). The methodology applied in order to calculate unit costs will thus be

auditable in the frame of a CFS or an official audit by the EC. The number of actual units claimed during the action must comply with the following conditions:
- the units must be actually used during the project
- they must be necessary for implementing the action & identifiable and verifiable, in particular supported by records and documentation.

How can evaluators assess the unit cost of a specific beneficiary? Do they have guidelines?

As this system is completely new, we have no information as to how the evaluators are briefed. Nevertheless, the calculation of unit costs must be based on recorded & certified figures and the methodology of calculation can be audited in the CFS / by the EC.

For a given consortium, can one beneficiary use unit costs and another real costs?

Yes.

Is compensation fee for the patients an eligible cost?

Yes.

How to calculate unit costs if the trial is a new process (was not carried out in the past)?

You would have to estimate as good as you can, based on information that is available and that has been recorded in the past. For example, even if that specific clinical trial has not been implemented at your site yet, you should be able to estimate the amount of time that your staff will spend per patient, and use the personnel costs from the last recorded year to calculate the personnel cost per patient included in this new study. All other components, such as consumables etc., should be calculated similarly.

Are "Research & Innovation Actions" funded 100% or 70%? I am asking concretely on PHC-14-2015.

100%

And what about costs of hospital care that we as a clinical trial sponsor have to pay?

Costs for hospital care that are paid through the national healthcare system/covered by health insurance cannot be charge to the project. Any costs for managing the patient that incur only due to the implementation of your project can be listed in the project budget.

In a clinical study involving different countries with very different actual cost levels, (personnel costs of doctors, other medical personnel and technical personnel) e.g. one very high, one very low, how can the unit costs be calculated to "be the same for all members of the consortium" as stated in 1.9 in the template for clinical trials?

For unit costs, the EC foresees different cost levels for different beneficiaries (see table in the template you are referring to column 3 & 4 + example provided in the table). While the total amount per unit can vary between beneficiaries of a consortium, the estimated effort

(e.g. time of a doctor spent per unit & amount of resources used per unit) must be the same for one trial, study investigation.

In another NCP presentation it says that it gives an exception to this rule for clinical trials - use of unit cost for in kind contribution...? Is the discussion ongoing or does it give a clear written statement on that?

It is possible to include study centres as 3rd parties providing in-kind contributions against payment. These third parties need to document their costs in the same way as beneficiaries (actual costs or unit costs). Please also see question 8 under "Consortium / Partners / Third Parties".

03_Approval (Ethics / Orphan drug)

Can Scientific advice and orphan drug approval from EMA (such as is required for CTs projects in the rare diseases program) be received from FDA instead, or must it be from EMA?

Approval needs to granted by EMA, but they offer a lot of assistance - contact them EARLY enough! The FDA approval might help as enabler/ door opener so you might receive Orphan drug designation earlier.

Does CT approval by the national ethics committee have to be included in the full proposal?

No. What might be helpful for your application: show that you have ethic committees at (some of) your partner institutions, show that you have experience with similar CTs in the past, or that you are already in discussions with ethic committee, and sometime an ethical board (with supervisory function) may be a good idea, if e.g. with transplanting organs, you have VERY sensible aspects.

Do you need to provide evidence of National or Institutional Ethics Approval for each partner involved in clinical trials at the proposal stage?

No.

Does the Ethics Approval need to be sent with the proposal? (Normally ethical approval will be sought at the early stages once the project has been approved.)

No.

04_Studies without drugs

It would be great if there was some mention of clinical trials which do not involve drugs, such as psychological therapy.

EC does not make big differences here. They clearly say (in the additional template) that they have a very broad definition of CTs - as long as you COLLECT human data (patients/

volunteers). Sure all we are presenting today is applicable for psychological therapy. Whenever a question in the template is not to answer, just write "not applicable".

If the therapy does not involve drugs, does the EMA need to be contacted? Is there another relevant organization which should be contacted?

Please see here for non-pharmaceutical products: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000202.jsp&mid=WC0b01ac0580024595. In general, we advise you to contact your national competent authority very early - and you might get great support from ethic committees located at your local/ regional university hospitals etc.

How would Usability Studies with Medical Devices fit in this scheme?

Please refer to the following presentation explaining that usability study is no clinical study: http://de.slideshare.net/Banderlin/usability-testing-medical-devices.

You are mainly talking about drug studies. Are there any topics where psychotherapy research is mostly recommended?

Not particularly.

05 Topic-related Questions

Is it compulsory to include clinical studies in Topics marked with an asterisk in WP 2015?

No, not compulsory (mandatory), but EC sees good chances that applicants will present "Concept & approach" where CT is a part of. If you will not conduct a CT in such a topic (*), please reflect on the budget. Of course the budget has been drafted to fund CT as part of the project.

Another question regarding PHC12: Are the evaluators in Phase 1 experts in Health issues? I raise the question because I now for a fact that a proposal for the development of an IVD without a biomarker involved has been funded, when a NCP told me that the diagnostic devices must always have to have a biomarker involved.

I understand the topic PHC 12 in a way that it can be and/ or medical device, so I would say, the evaluators have decided accordingly**.**

Is clinical trial mandatory in PHC18? What can be the duration of PHC18?

The topic says “based on clinical trials and/ or real world data”. Duration depends fully on your concept and approach.

For PHC14, is it mandatory to have received a response on EMA protocol assistance, prior to the submission of Stage 2 application?

Yes, and as topic says: you should have granted the orphan drug designation at the time of

stage 2 submission.

Is CT documentation also necessary for the SME call PHC-12?

Yes, but not in a separate template.

I am surprised that PHC12, which is specifically based on a clinical validation, does not include a clinical template, could you please confirm this?

Yes it is correct that for PHC 12, the clinical trial template is NOT mandatory. Info regarding the trial needs to be included in the main template (= Part B).

06 Consortium / Partners / Third Parties

Giving the fact any Horizon project involve a consortium maybe it will be useful that participants in this webinar share their email address and key interest for finding potential partners.

There is a partner search tool on the FFH2.0 website which you may want to check out for this purpose:
http://www.fitforhealth.eu/user?ReturnUrl=http%3a%2f%2fmm.fitforhealth.eu

What is the opinion of the EC on CRO being a partner in the consortium, with its core task of documentation preparation and quality control and Quality assurance?

It is possible to include a CRO.

Can CROs or recruiting sites be named as subcontractors or is this still subject to the normal subcontracting rules about openness, transparency and cost effectiveness?

No and yes, the task to be subcontracted must be named in the application, but not the name of the subcontractor. For any subcontracting, respect the guidelines on procurement (European, national and of your institution).

What does "too much" subcontracting means? Will it depend only on the evaluators' criteria?

"Too much" is not budget-wise. It is referring to amount and scope of tasks: how central/ crucial is the task you are going to subcontract, compared to the rest of you project?

Could you explain a bit more the in kind contribution option against payment? Why can we not use unit cost for this?

That is what EC told us. Sorry we do not know more on that.

Does the rule of not subcontracting of core tasks also apply to PHC12, which is SME Instrument? A small biotech or IVD company might not have the capabilities to conduct the CT, so it must be obliged to subcontract them entirely.

The clinical study partners should be partners= beneficiaries whenever possible, this is right; but in PHC12 only SME are eligible for funding. So you either can identify a for-profit CRO that is willing to act as beneficiary (as it is 100% funding rate this is not too bad), or they act as subcontractor. If you are or prefer working with non-profit CROs or with academic partners (university hospitals), they must be subcontracted for this topic. The commission is aware of the dilemma, but confident that the amount of subcontracting will not be a major hurdle for the applicants respectively the evaluation result. Note that in PHC12 like in any other SME instrument topic, the "impact" is even more important than in research & innovation actions, compared to "excellence". This is: plan and write your project proposal in the best way for your company so that you will be able to become a champion in your market.

We are a SME in Barcelona. We have experience in several FP7 projects, developing the recruitment database for patient's data collection. I don't know where to find Institutions and other partners that can be interested in such a partnership.

Please have a look at the FFH website: http://www.fitforhealth.eu/news/new-fit-health-20-partner-search-and-matchmaking-tool-online.

If we have around 10 different recruiting centers, should we include them as beneficiaries or subcontractors?

Including them as a beneficiary is always the preferred option. However, subcontracting is also possible. This has to be decided individually for each project. The document "Frequently Asked Questions" concerning the Horizon 2020 societal challenge "Health, demographic change and wellbeing" says: Every clinical center can be a beneficiary, and the Commission will not oppose or discourage a large number of beneficiaries for this purpose. Alternative ways to include and reimburse such clinical centers are:
(i) As third parties providing in-kind contributions against payment (Art. 11 of the grant agreement). A requirement for this is a written agreement between the beneficiary and the third party prior to the start of the work. These third parties need to document their costs in the same way as beneficiaries (actual costs or unit costs). Wherever possible, third parties should be listed in section B4.2 of the full proposal.
(ii) As subcontractors (Art. 13 of the grant agreement). In this case, the beneficiary needs to ensure that it complies with the obligation to ensure the best value for money and institutional rules for subcontracting and if the beneficiary is a public body, with national and EU legislation on public procurement. Subcontractors would not usually be named in a proposal given the necessity to undertake the processes required to ensure compliance with the conditions described above. If however such processes have been undertaken in advance, subcontractors may be named in a proposal.
(iii) Another option, to participate as 'linked beneficiary', is limited to entities that fulfil the specific conditions of Art. 14 of the grant agreement on 'affiliated entities and third parties with a legal link to a beneficiary'. As these conditions are rather specific, the use of this option is likely to be limited.

07 Proposal Structure

Is part 4 used by the experts for evaluation, or do they have to disregard it (only to assess the capability of the consortium).

Evaluation criteria are applied for chapters 1-3 only. As I mentioned, I would put as much info as possible into the chapters which are not page limited, but you should of course MENTION them in chapter 3 as well (and make reference to the extended versions).

Is it possible to just give a few information on the CT in the file that we submit, as our clinical development will be conditioned by the preclinical data that we will obtain?

Yes, you give as many details as you are able to give at that moment. The later the CT will happen, the less details you will know at the time of application. Evaluators need to be convinced, nevertheless, so at least give a vision of your idea.

08 Project

What are the consequences if you do not finish your project / clinical study in the time that stands for the particular PHC?

EC told us that a cost-neutral prolongation of EU projects will be more difficult now, compared to FP7. I would say that in worst case, you will not be able to deliver all deliverables that you are committed to (Grant agreement), so that you might lose some of the final funding portion.

Based on the points made about time planning would you expect the duration of a project including clinical trials to be longer than those under FP7, for example, 6 years instead of 5? Do you think this will be accepted by the Commission?

With regards to "realistic" 6 years might be better than 5 years – so you need to argue accordingly. With regards to credibility and manageability – I would not recommend to prolongate the projects too much. The longer a project is, the more may happen meanwhile which affects results etc. You might rather consider to leave out 1 or 2 Work steps and make the project more tiny and focused.

At the stage of the application, documents like informed consent form, information sheets, ethics approvals etc. are not available yet. These will often be established during the project. How should one deal with that?

Say as it is – we have this, we are here, but xyz is not yet precisely projectable.

It was said that no major changes should be made between step 1 and step 2. What is considered as major changes?

There is no EC definition of 'major change'. It is up to the evaluators to decide whether a change is significant or not. In some calls (e.g. LEIT-BIO; SFS), consortia were asked to list

any substantial differences between the 1st stage & 2nd stage proposal (i.e. changes with regards to partnership, budget, approach, workplan) and indicate the reasons in the proposal submission forms.

09_Other

Can you advise as to how sponsorship should be dealt with for the clincial trial?

The sponsor should not have significant say in the study protocol so that it will still be seen as “investigator initiated”; also, sponsor shall not have access to raw data/ uncoded data.

++++++++++ Disclaimer: This is not a legally binding document. ++++++++++