Fit for Health 2.0

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

Clinical trials management in Horizon 2020 projects

www.fitforhealth.eu

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Dr. Claudia Schacht | Eurice GmbH

What is a 'clinical trial' in H2020?

→ DEFINITION:
('Template for essential information to be provided for proposals including clinical trials / studies / investigations')

A 'clinical study' as 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).

→ SCOPE:
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

Characteristics of these clinical studies

- work with patients
- collect samples and/or data from patients
- special part of your project with certain characteristics that are different from rest of your project / ‚classical' collaborative project

Challenges of these clinical studies

- Timely patient recruitment and management
- Data collection and management
- Financial management
- Integration into rest of the project

Why clinical trials?

The implementation of clinical trials in a collaborative, transnational approach has a **clear European added value**:

- easier to reach sufficient patient numbers (especially in the case of rare diseases and stratified treatment groups)
- faster recruitment rates
- consolidated expertise

In addition, clinical trials are the **ultimate validation step for any innovation in clinical Health Research**, bringing innovations to markets and patients – one of the main objectives of Horizon 2020.

Typical challenges

Project extensions

- **Communication by the EC on "Restrictions on extensions to the duration of grant agreements, and respect of reporting deadlines" (June 2014)**

  […] recent experience has shown that **nearly 50% of grants are not completed in the timescale set out in the Grant Agreement**, but are extended through an amendment. This level of amendments shows that it is no longer the exceptional procedure that it was intended to be, but has become a common practice in the 7th Framework Programme. For this reason, the Commission services will, in future, more closely examine each request for an extension to the duration of the project to ensure that they are only given where there is a clear added value for the project, or where external events (not reasonably foreseeable at the point of signing the grant) mean that it is impossible to complete the work in the agreed timeframe.

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR RESEARCH & INNOVATION

Brussels,
DG RTD/R3

NOTE TO COORDINATORS OF PROJECTS UNDER THE EUROPEAN COMMISSION'S 7TH FRAMEWORK PROGRAMME

Subject: **Restrictions on extensions to the duration of grant agreements, and respect of reporting deadlines**

In accordance with the FP7 Grant Agreement it is an obligation of the consortium of beneficiaries to carry out the work as identified in Annex I (Article II.3.a)) and within the duration of the project fixed in Article 3. Reports and deliverables should be provided within the deadlines set in Article II.4 of Annex 2. In accordance with FP7 policy the consortium may request the modification of the duration of the project to the Commission via an amendment.

An extension to the length of a Grant Agreement delays the availability of research results and their dissemination and exploitation. So while they may be necessary in certain cases they are clearly not desirable and should be kept to a minimum.

Typical challenges

Even among 'regular' FP7 projects:

- ~ 50% of grants were not completed in time & had to be extended through an amendment

Clinical trials

- are known to be particularly complex
- literature: up to 85% of clinical trials in general are not completed in time
- most common reasons for delays: site initiation and patient recruitment
- often leading to cost increase

Typical challenges

H2020 project + clinical trial → 'double challenge'

BUT

- maximum EC contribution per project is fixed
- timely completion of projects / quick translation of research results into application is a declared goal under Horizon 2020

To help overcome these challenges, the European Commission provides clear guidance on how to optimally plan and describe your study in the proposal phase, and has adapted their financial rules in appreciation of the special requirements of clinical trials (→ "Unit Costs").

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‘

3) 'Report on status of posting results' in the study registry(ies)

Management issues

1. **Before start of study**
   - Protocol development
   - Ethical approval
2. **During study implementation:**
   - **Working with patients**
     - Patient availability / recruitment delays
     - Financial issues
   - **Data collection**
     - CRFs
     - Data entry/integration, QC
3. **Conclusions & useful links and reference documents**

Management issues

1. **Before start of study**
   - Protocol development
   - Ethical approval

Management issues: site initiation

Protocol development

- Harmonized study protocol across sites needed to start the work
- Only outline of protocol required in proposal

Ethical approval

- Not required for proposal submission, but indispensable for uptake of activities
- H2020: very short time to grant!

If not in place already: Designate one person in charge who will drive protocol development and ethics applications instantly. (Note that costs for related activities can only be reimbursed if they occur during project duration.)

Final protocol & ethics approval = mandatory deliverables

Management issues

2. **During study implementation:**
   - **Working with patients**
     - Patient availability / recruitment delays
     - Financial issues
   - **Data management**
     - Data collection/CRFs
     - Data entry/integration, QC

Management issues: working with patients

Patient availability / recruitment delays

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

Management issues: working with patients

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- **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

Management issues: working with patients

Financial issues

- sites may not be aware of or experienced with the principle of reimbursement/instalments/negative cash flow
- high workload, large number of individuals involved per site, continuity must be ensured
- shifting of activities related to patient recruitment is common
- if patient numbers significantly lower than expected in one site: prepayment exceeding max funding?
- unit costs or subcontract option were created to increase flexibility

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- shifting of activities related to patient recruitment is common
- if patient numbers significantly lower than expected in one site: prepayment exceeding max funding? **Reduce risk by opting for instalment option in CA**
- unit costs or subcontract option were created to increase flexibility
- **know the system and typical challenges to minimize risk & optimize your project**
- **provide close support to recruiting centers**

Management issues: working with patients

Financial Issues: Unit Costs

Special financing rules to accommodate clinical trials in H2020

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.

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

Management issues: working with patients

Financial Issues: Unit Costs

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MUST READ!

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

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.
- Unit costs are a simple and transparent method for calculating, reimbursing and auditing costs of clinical studies.

Unit Costs - Conditions

- Alternative to the use of actual costs, on voluntary basis
- Only one of the forms, actual costs OR unit costs, may be used for one clinical study for one beneficiary or linked third party
- Resources and costs will be evaluated with the proposal
- Unit costs per patient/study subject fixed for the entire duration of the project

How to calculate Unit Costs

Per clinical study subject: Estimation of the resources

- per task on the basis of the protocol,
- the same for all beneficiaries involved (applying unit costs).

Per beneficiary/third party: Calculation of costs based on its historical costs:

- recorded in its certified or auditable profit and loss accounts,
- for last closed financial year at the time of submission of the proposal.

Verification and audit ex-post only:

- number of patients/subjects declared = number of patients/subjects actually participating in the study
- Beneficiary/third party has used the accounting data of year N-1.

Unit Costs - the component ‘personnel costs’

3 unique and exclusive personnel categories:

- Doctors
- Other medical personnel
- Technical personnel

No other personal category / calculation base for personal costs possible

(e.g. separate categories for 'nurses‘, 'study nurses' or 'pharmacists' do not exist)

Unit Costs – practical tips to minimize risk

- **Underestimation of costs involved**

Have an experienced clinician together with an experienced project manager set up your unit cost system. Plan enough time for several rounds of circulation and of feedback to the elements involved by all sites.

- **Loss of funds due to drop-outs**

Possible to divide into steps (e.g. recruitment + intervention one, intervention two, follow-up).

- **Loss of funds after audit**

Pay utmost attention that beneficiary/third party has used the accounting data of year N-1. No cost estimates! This is different from the 'usual' H2020 budgeting process. Make sure sites involved understand. Mistakes in this step of the planning process may result in significant loss of funds for the respective site.

Management issues: data management

Data collection/CRFs

- paper and/or electronic version (PC vs mobile devices)
- 'mainly established' vs 'new system'
- changes during the project difficult/impossible

Data entry/integration, QC

- key to secure generated data and ensure their usability
- only data that are in the database can be processed → bottleneck
- option: dedicated data entry clerk

DMP: rules and procedures for data generation & data management, for clinical and other data

Management issues: data management

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- **ensure sufficient training of personnel** who will be filling out the CRFs

Data entry/integration, QC

- key to secure generated data and ensure their usability
- only data that are in the database can be processed → bottleneck
- option: dedicated data entry clerk
- **ensure sufficient training of personnel** who will be entering the data
- **implement continuous monitoring/control mechanisms**
- **keep an eye on the time needed for completion of following tasks to determine data entry deadlines**

Management issues

3. **Conclusions & useful links and reference documents**

Concluding remarks

Timely completing of planned work is particularly challenging in clinical studies

Tips for Minimizing Delays

1. **Start work immediately** to ensure timely site initiation
2. **Revisit site assessment regularly** – Review/obtain key operational criteria and information on administrative capacity to optimize calculations of expected patient distribution (continuous process)
3. **Adapt your project management approach** - Structures and activities need to acknowledge the inherent variability of the process and allow for quick identification of difficulties, and prompt changes/adaptations during implementation
4. **Build relationships** – the responsible project management team must create an authentic, responsive relationship with each of the sites. Site visits early on often pay off in the course of the project.

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/sc1-hco-07-2017/1730125-faqs_v5_august2016_en.pdf
- EU IPR helpdesk: www.iprhelpdesk.eu
- ECRIN: http://www.ecrin.org/ helpful info and tools on website, and diverse trial support services to their nine member countries
- FFH 2.0 support

Thank you!

Dr. Claudia Schacht | Eurice GmbH

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