

BeNeFIT budget tool guidance notes

Introduction

The BeNeFIT call is a unique collaboration between ZonMw and KCE Trials to fund comparative effectiveness trials in Belgium and the Netherlands.

To facilitate the selection process and funding streams, candidates should submit the trial budget using the standardised [budget tool](#) designed for this call.

The budget tool integrates the ways of working of KCE Trials and ZonMw and is only to be used for BeNeFIT international calls. For national calls, the local organisational rules still apply.

For the BeNeFIT call, the tool differentiates between sponsor costs and site costs. All sponsor costs will be split between KCE and ZonMw, who will each pay 50% of the sponsor costs. Site costs will be paid by the funding agency of the respective country. Site costs can differ by country due to price differences and more importantly, due to the number of recruited patients per country. Therefore, a balanced number of recruited patients in the two countries is encouraged. Proposals with a balanced representation of Belgian and Dutch centres (and for Belgium, a good representation of Dutch and French speaking centres) will be prioritised.

There is no pre-set maximum budget per proposal other than the call budget limits. All necessary costs will be covered if justified in the completed budget tool.

As you will see, the budget is constructed based on tasks that need to be performed rather than on an estimated FTE basis and contains pre-automated formulae related to the study parameters. Once completed, an estimation of the FTE needed will be calculated automatically.

We expect you to submit a draft completed budget tool along with the research outline (RO). Candidates who will be invited to submit a full research proposal (FRP) will receive first comments on the draft budget, that need to be taken into account when submitting a revised budget with the FRP. The final budget should not deviate more than 15% from the original budget submitted at the RO stage (unless this is requested in the decision letter).

The budget tool and guidelines are developed by KCE Trials. If you wish to use this budget tool outside the KCE Trials Programme or the BeNeFit call, you should contact trials@kce.fgov.be.

Tell us how and why you wish to use the tool. Please include your contact details: name, institution/company, address, telephone number, and email.

Guidance to complete the BeNeFIT budget tool

These guidelines refer to version 1.0 date 16/01/2018 of the BeNeFIT [budget tool](#)

The budget template consists of different tabs detailing the study parameters, budget parameters, the sponsor costs, site costs and the overall costs. Extra tabs can be used if needed, for example to detail the costs of a contractor/collaborator. **The budget template is pre-filled with study related tasks but will need to be adapted according to each specific protocol.** Lines and tasks can be deleted or inserted as appropriate, however the general principles of the type of tasks allocated to a subheading should not be changed.

For general tasks a fixed price (FX) has been determined. Where relevant, formulas related to the study parameter have been inserted. Note that only in very rare cases for non-standard studies the fixed amount may be adapted after justification from the sponsor.

COLOR CODING

GREEN: DO NOT CHANGE

Cells in **green** contain formulas and are automatically calculated based on cells completed in other parts of the excel sheet. **You should not change a figure in green.** By adding information elsewhere e.g. in the study parameters tab, this figure will be updated automatically.

YELLOW: YOU NEED TO COMPLETE

Cells in **yellow** need to be completed to allow for automatic calculations throughout the worksheet.

This guideline document gives instructions on each of the tabs. Additional information is provided in the 'how to complete' tab of the budget tool excel file.

For questions related to the budget tool, please contact trials@kce.fgov.be.

STUDY PARAMETERS

In this tab, the general information about the trial and the trial timelines should be provided. Some of the information in the cells will be automatically transferred to the other worksheets. Do not insert or delete lines in this tab as the links to the overall costs might no longer work.

- Trial Number: to be completed once a trial number has been assigned by the BeNeFIT call secretariat.
- Planned number of subjects (screened, randomised, completed)
A screened patient means a patient that has signed informed consent and was formally asked to participate in the trial. As pragmatic trials have only a limited number of inclusion/exclusion criteria, the number of patients screened is not expected to differ much from the number of patients randomised.
In exceptional circumstances, where a high drop-out rate during the study can be expected, the number of patients completed might have an impact on the budget. In that case this should be reflected in the tab site visit costs. E.g. if a high drop-out rate is expected, only a % of patients will perform all visits (less monitoring, medication,... required for the follow-up part).
- Number of protocol related visits per subject = the number of visits where data collection will be performed including the standard of care visits (therapy sessions that do not require data collection points are not to be included)
- Number of sites
- Study timelines
 - FPI: First Patient In (first patient signed informed consent)
 - LPI: Last Patient In
 - LPLV: Last Patient Last Visit
 - DBL: Database Lock
 - CSR: Clinical Study Report
- Note that the time between LPLV and CSR should not exceed 6 months.
- The on-site and off-site monitoring frequency (if relevant) needs to be determined as well as the number of CRAs on the project (take into account back-up CRA, note that having 2 CRAs does not necessarily mean 2 FTEs) – the monitoring frequency should be defined after a thorough risk-assessment of the trial and should be justified in a monitoring plan. The number of visits here does not include the initiation and close-out visits (mentioned on separate lines in the tab sponsor costs).
- Planned number or monitoring visits abroad (fixed cost per visit abroad). Depending on the sponsor country this will be number of sites in BE or NL and will also depend on decision of outsourcing monitoring to a coordinating centre in the other country.

The timelines for the study start at the milestone “first patient in”. Time that is invested in tasks before that date are included in fixed prices. The sponsor can ask for an advance payment (€ 12 500) to help support the development of the protocol if a proposal is invited to submit a full research proposal (FRP). A second advance payment (€ 12 500) can be requested to support the required additional recruitment check, as stated in the call text. These upfront payments are part of the budget, however if the study would not be selected for funding, the advance payments do not need to be refunded by the applicant.

Trial timelines should be estimated for the analysis and reporting of the primary endpoint. In cases where the data collection time points for secondary endpoints deviates considerably (e.g. > 6 months) from the primary endpoint, a separate budget should be developed and included as an additional excel sheet/tab in the file. It should reflect the less intense follow-up for the period and tasks involved in this long-term follow-up for secondary endpoints.

- Expected number of reportable SAEs
Note that in a pragmatic trial, the expected number of SAEs should be based on the safety reporting requirements in the protocol (which are in turn based on the risk assessment).

BUDGET PARAMETERS

In this tab the standard hourly rates/fees for the different roles involved in the study are mentioned, based on hourly rates used by KCE Trials and ZonMw. The rate for the CRA has been adjusted to include transportation.

We recommend that you use these rates to build your budget. In case an individual rate is higher because of seniority, we consider this will be counterbalanced by the margin as well as lower individual rates for other roles.

The aim is that the estimation of the number of hours per activity by the sponsor and the sites should be as accurately as possible (not underestimated nor overestimated). In addition, we added a margin of 10% to account for future indexation, unforeseen delays and extra costs or capacity needs during the study. Note that for items with a fixed cost no margin should be added.

OVERHEAD

No overhead is to be included in the budget of BeNeFIT studies.

VALUE ADDED TAX (VAT)

The VAT that is applicable to research activities should be checked in this tab. It is indicated at 21% at the time of publication of this guideline. Make sure your total budget is VAT included.

The start-up costs for the site are set at €1.000. It should cover the costs for the site involved in the preparation for the initiation of the study (contracts, training, site set-up). This amount will be lower if working with GP sites (suggested fee of €200) and can be higher if working in a very complex setting involving several departments, pharmacy, lab etc. Any adjustment to the start-up costs should be justified.

📁 SPONSOR COST

General Guidelines

The number of suggested hours for each task are real life estimates and should be sufficient to cover the task. Several factors such as the complexity of the trial, the location and organisation of the participating sites (e.g. GPs, hospitals, presence of trial nurse,...) will drive the costs. **A 'reality check' of the total amount of each section is part of the budget building exercise.**

It is not the intention that the maximum suggested number of hours is used as a general rule. Sponsor teams will have to justify the time they think is needed.

We have populated the grid with roles (team member column) that are relevant to the performance of each defined task. This allocation is not mandatory to follow and can be changed according to the organisational structure or the type of trial. However, the tasks undertaken by a role should be appropriate for that role; all activities that can reasonably be delegated should be delegated to people with the necessary profile, experience and qualifications e.g. a junior PhD student should not be given the role of Project Manager for a multicentre RCT and, vice versa, a senior Project Manager should not be doing tasks that can be done by an administrative assistant.

FIXED AMOUNTS

For several tasks, a fixed amount (FX) has been calculated that represents the total of the time invested by the different roles. E.g. project design and set-up include protocol development where the Investigators, Project Manager, Statistician and Health Economist are all involved. The total estimate of the time and costs related to this have been integrated into a fixed amount. (FX in the team member columns).

Depending on the study setting (e.g. hospital based, GP practices, specialist centres) the time needed may vary. The grid has been developed for a low/medium complexity (based on data points and safety) trial in a hospital setting.

1. Project Design and Set up

This section includes all activities that are performed to enable the set-up of the project and that are required before the project undergoes regulatory/ethics review. There are two parts in this section: one fixed and one variable, based on number of sites to be visited.

Section 1a FIXED AMOUNT:

This fixed amount includes the following:

- Development of the protocol (including patient and public involvement, statistics, health economics, internal and external review, ...); in case experts are consulted, the cost for travel, etc. should be covered by this amount
- Development of patient related documents (e.g. Patient Information Sheet and Consent Form, specific questionnaires, ...) including any translations
- Development of agreements with funder, vendor/contractors
- Costs for review of documents related to this section
- Initial selection of participating sites/GPs

The feasibility of the study depends on the number of sites to be visited. In the current pre-populated grid, all sites are scheduled to have an on-site feasibility visit. For large scale trials, this will not be possible and this line should be adapted. E.g. a full site feasibility visit in 10% of the sites and remote feasibility check in other 90% of the sites (€200/site).

The conduct of the feasibility and site selection visits is the responsibility of the sponsor. In addition, we will ask a contract research organisation (CRO) to complete an additional check of recruitment feasibility (see call text). Where appropriate, the sponsor feasibility visit and the CRO visit to the site can be combined.

The set-up, negotiation and finalisation of agreements with sites will depend on the number of sites involved. In case GPs are involved or in situations where there is no negotiation with hospital management required, the fixed amount for the contract development and negotiation needs to be reduced.

License fees for the use of questionnaires are to be included in this section. However if an app, IT platform or another tool is developed, the costs for this should be detailed in section 12a, study specific equipment unless they are integrated in the eCRF platform.

2. Regulatory and Ethics Review

This section should include all costs that are related to:

- Development of medicinal product/device related documentation including IMP label related activities (design, translation), if applicable and if needed for regulatory/ethics review
- Submission of the dossier to the Ethics Committee(s)
- Submission of the dossier to Competent Authorities, if applicable
- Provision of insurance, according to the legislation. You need to check with your insurance department if your institution already has undertaken an insurance policy that covers this.

3. Monitoring

This section should include the cost for the monitoring of the trial as specified in ICH-GCP E6 (R2) 5.18 and should take into account a risk based approach. The monitoring of a low-risk, pragmatic trial will require less frequent on-site monitoring visits and can even be done completely centralised.

The development of a monitoring plan (fixed amount) and all costs related to the implementation and follow-up of the study at the participating sites are to be covered in this section:

- Training of CRAs: this is the time needed for the CRAs to study the protocol and get familiar with the disease area. It is not the training that is delivered to the sites (this is included in initiation visit and investigator meeting)
- Conduct of initiation visits. The suggested time (16 hours) needs to be adapted in case of remote initiation, investigator meeting counting as initiation visit or blended formula. Also the complexity of the trial and the involvement of different departments will need to be taken into account; e.g. time needed for an initiation visit at a GP practice will be considerably lower than a trial which involves different hospital departments, pharmacy, lab etc.
- Conduct of on-site monitoring visits
- Conduct of study closure

- Any remote monitoring activities: for this activity, the formula contains 4 hours per contact per site but the time will highly depend on risk assessment, number of patients and number of data points. The formula should be adapted depending on the monitoring plan – this activity can be split between data manager or CRA.
- Travel costs abroad for monitoring visits (fixed cost per visit to cover extra costs like transport/hotel costs)

The time allocated to each activity in this section is for a study of medium complexity. It should be adapted for studies of low complexity and should be justified in a monitoring plan.

4. Quality Assurance

Section 4 FIXED AMOUNT:

This fixed amount has been calculated for a 2 day sponsor audit and 2 day visit on site including preparation, reporting and follow-up.

This activity should be taken care of by an independent quality department. It can be the quality department of the hospital or can be outsourced. The cost for the outsourcing of this activity should be covered by the amount in this section.

5. TMF Handling & Administration

- This section includes all administrative activities related to the documentation, collection and archiving of essential documents: set-up and maintenance of a (e)TMF, (e)ISF, set-up and maintenance of a study portal.
- A fixed amount has been calculated for the general set-up.
- All activities that are dependent on the number sites involved, are mentioned on separate lines.
- If extra budget is needed for shipments of study material (e.g. in case of a fully remote study initiation) this should be included on a line 5c “Shipment and Distribution Services”.
- This section includes the administrative work involved in the set-up, execution and follow-up of invoices and payments by the sponsor. This needs to be adapted according to the agreed number of payments and depending on the trial setting (could be once yearly).
- Archiving costs

6. Safety

This section includes all activities related to the evaluation of the safety of the intervention studied (IMP, device, procedure, ...).

Note that if working with a registered drug in an approved indication, safety reporting will follow the routine reporting for drugs with marketing authorisation.

Section 6 FIXED AMOUNT:

This fixed amount includes:

- Set-up of safety database
- Follow-up of reportable SAEs (SUSARs or SAEs as specified in the protocol)
- Writing of SUSARs (if IMP)
- Reporting to EudraVigilance Database if IMP or materiovigilance reporting if device
- Meetings on safety findings with DSMB if applicable (if IMP, can be Steering Committee otherwise)
- Reconciliation of the safety database

7. Data Management

This section includes all activities related to the data management for the clinical trial. Keep in mind that the number of data items collected should be kept to a strict minimum and should only address the research questions in the protocol. All data collected should be analysed.

In case the study runs over a long time (>4 years), additional budget might be required for data management activities.

Section 7 FIXED AMOUNT

This fixed amount includes the following:

- Design of eCRF
- Design of Clinical Trial Database
- Writing of the Data Management Plan
- Data Coding of adverse events (if applicable)
- Data Coding of medication (if applicable)
- Programming of queries (and sending in batches)
- Running query batches and distribution to sites
- Follow-up on query resolution
- Import of data (ECG, lab, images, ... if applicable)
- Database lock

The fixed amount proposed makes a distinction between a trial of low complexity and a trial with moderate complexity. The distinction between low and moderate complexity should be based on the number of data points and the required safety follow-up.

8. Statistics, report and publication

This section includes the activities related to the statistical analysis for this trial, from statistical programming to collaboration between statisticians and clinical team to write the clinical study report.

Statistical input at the study set-up (including activities related to the randomisation process) is already budgeted under section 1.

Section 8 FIXED AMOUNT

This fixed amount includes the following:

- Statistical programming
- Generation of tables and listings
- Development of a Statistical Analysis Plan
- Statistical analysis and reports
- Generation of the Clinical Study Report, including meetings and review
- Writing and submission of the publication
- Any costs to ensure open access to the main publication of the study

Note that:

- Any subsequent analyses and publications are also included in this budget
- Any investigator meetings planned to present the trial results should be included under section 9, Project Management

9. Project Management

This section consists of the project management activities that are not mentioned in any of the above sections. It takes into account the time needed for the generation of study specific documents (communication plan, development of newsletters,...), the day to day follow-up of the trial (contact with key stakeholders, planning of meetings, follow-up of recruitment, follow-up of budget ...). Costs related to activities detailed in the other sections need to be included in their respective sections rather than attributing them to the role of PM in this section (e.g. development of regulatory documents need to be included in section 1 or section 2).

Time for meetings that are not linked to any of the activities in the other sections, need to be planned in this section.

- Project Management, other
 - o As an example, time needed for day to day follow-up for a study for 1 year is estimated as 0,5 FTE. This example can't be considered as applicable to every trial and needs to be adapted case by case.
 - o Include the motivation for the time estimated for project management according to the setting of your study.
- Project Status Reports (reporting to the funder); during the recruitment phase of the study, regular updates are required. In a 2nd line, the less frequent reporting after the recruitment period is captured.
- Investigator Meeting(s)
- Steering Committee Meeting(s): time and travel for external attendees and PPI representatives (patient and public) should be covered by the fixed amount

If large investigator meetings have to be held off-site, costs for meeting room and catering are to be listed in the "external costs", a fixed amount for this has been calculated (line 11d)

10. IMP/Intervention Handling

In case the study requires a specific Investigational Medicinal Product, a device or a special intervention, all costs for purchasing, labelling, developing, tracking, etc. need to be included here. As comparative effectiveness trials are pragmatic trials, efforts should be made to prescribe and invoice medication or other interventions as in routine practice.

- IMP or intervention accountability, will vary for pragmatic trials: this includes the time needed by the pharmacist to perform all IMP related tasks
- Cost for IMP, comparator/placebo, device, ... (including import license if applicable)
- Storage, distribution, maintenance
- Packaging, blinding, labelling
- IMP destruction & recovery unused products

This section is not pre-filled as it will highly depend on the type of IMP/device/intervention. In case IMP handling is totally outsourced, it should still be captured in this section.

11. External vendors/contractors and central review

All costs related to the outsourcing of activities that do not relate to any of the above (e.g. central review, ...) should be included in this section.

This section should also include costs for any specific equipment that needs to be purchased for the study. It should not include material needed for the day to day business of the personnel working on this study (e.g. PC, printing, paper, ...)

Costs related to the catering and room rental for an investigator's meeting need to be detailed here. If deviation from the fixed amount this should be justified.

SITE COSTS

In this tabs an overview of protocol specific tasks should be generated. A specific tab has been created for each country.

Consideration should be given to the standard of care in each country. The sponsor team should determine the standard of care related to the frequency of follow-up visits, reimbursement criteria for the intervention and for any protocol related investigations. Activities that are considered as standard of care cannot be charged to the study budget.

As comparative effectiveness trials are pragmatic trials, the data collected should come from routine medical data. However study specific costs (Informed Consent discussion, investigations, pharmacy, ...) and time spent for the administration and data entry can be included here.

As a standard, the non-procedure section takes into account an average estimated time required by the study nurse and local investigator for the administration and follow-up of a pragmatic clinical trial which should be limited to data entry tasks and time needed for monitoring. In case safety follow-up is needed in addition to the normal pharmacovigilance for marketed products, this should also be added.

Start-up costs for sites are taken from the budget parameters tab.

If you have any questions please don't hesitate to contact Trials@kce.fgov.be