Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

KCE Belgian Coordinating Centre (BCC) budget tool guidelines

These guidelines refer to version 2.0 date 29/06/2018 of the KCE BCC budget tool.

This budget tool has been developed for international trials where part of the sponsor tasks are delegated to a Belgian centre.
The aim of the budget tool is twofold: first, to make sure the applicant considers all necessary trial activities for the budget; second, to facilitate a fair and similar compensation across the trials funded. It remains however a tool and individual trials may have specific budget needs that need discussion on a case by case base.

Only the tasks that are delivered by the Belgian Coordinating Centre are to be budgeted. A document detailing the delegation of tasks as well as the funding from other funding bodies, should accompany the budget table. E.g. If the protocol is developed by the international team, the costs for the Belgian Coordinating Centre will be limited to the development of the Belgian Patient Information Sheet and Consent Form, local translations, … and not the protocol development (including statistics, health economics, …) in itself.

Although in the early stage of a project, it might seem difficult to complete the budget tool, we expect candidates to consider the different parameters and tasks in making a first draft budget. The initial budget will be considered ad draft during the initial selection steps and will not be a selection criterion at this stage. This budget is still subject to change between the different steps of the submission process (from outline to recommendation for funding and final contract). The final budget will be the result of changes to the research proposal based on input from the Trials Board and budget negotiations with the KCE Trials Team and will need approval by KCE Board.

For international studies when the sponsor is in Belgium: The extended version of budget tool should be used to calculate the costs.

Regarding patient fee, it should detail what the distribution will be regarding patients included in Belgium and patients included in other countries.

The budget template consists of different tabs detailing the study parameters, budget parameters, the overall costs and the site 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 amount (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 by KCE after justification from the sponsor.

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

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

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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

Rows that are grey shaded can be used to detail the budget that the international sponsor has allocated to that task.

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

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. In case your project would require additional lines, please contact Trials[@]kce.fgov.be to discuss.

- KCE Reference: the KCE Reference number is assigned when the project is recommended for funding by the Trials Board and can be found in the Trials Board decision letter, e.g. KCE-18001
- Planned number of subjects (screened, randomised, completed) in Belgium
  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 site visit costs.
- Number of protocol related visits per subject = the number of visits where data collection will be performed including the standard of care visits
- Number of sites in Belgium
- Study timelines
  - FPI: First Patient In in Belgium (date the first Belgian patient signs ICF)
  - LPI: Last Patient In in Belgium
  - LPLV: Last patient Last Visit in Belgium
  - 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)
  KCE expects that as a minimum quality check, all Informed Consent forms and patient existence will be verified in all participating sits. Regarding the primary variable as far as not reported by the patients themselves, source data verification should be documented according to the monitoring plan.

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 pricesor is assumed to be taken care of by the sponsor team.

Trial timelines should be estimated for the analysis and reporting of the primary endpoint. Additional longer term endpoints and subsequent publications should not be included in the timelines.

🗀 BUDGET PARAMETERS

In this tab the standard hourly rates/fees for the different roles involved in the study are mentioned. These rates are largely based on KCE report 178 https://kce.fgov.be/publication/report/manual-for-cost-based-pricing-of-hospital-interventions that analysed the cost of personnel working in hospitals. Based on a yearly number of hours of 1976 and taking into account paid holidays (24 days), public holidays (10 days), education and training (3 days), sick and accident leave (7 days) and other absences (5 days) the number of productive hours is estimated at 1605.2 hours. The rates have been adjusted for indexation and include the 2017 indexation. The rate for the CRA has been adjusted to include transportation. KCE recommends that you use these rates to build your budget. Exceptions are possible in very specific circumstances, but should be justified by information from the university/hospital HR department and are subject to review and prior agreement by KCE. In case an individual rate is higher because of seniority, KCE considers 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, KCE has added a margin of 15% to account for future indexation, unforeseen delays and extra costs or capacity needs during the study. This is to support the learning curve in the first years of the KCE Trials programme. Note that for items with a fixed cost no margin should be added.

OVERHEAD

KCE accepts a maximum rate of 17% for overhead costs.

Adding full overhead costs for expensive fixed cost items (>10.000 EURO) may not be appropriate and will require discussion on a case by case basis.

There is no overhead for the sponsor on the site costs, however overhead costs charged by sites with a maximum of 17%, can be included.

Cfr. Advance to be discussed

The start-up costs for the site are set at €1000. This amount will be lower if working with GP sites (suggested fee of 250€) and can be higher if working in a complex setting involving several departments, pharmacy, lab

etc. It should cover the costs for the site involved in the preparation for the initiation of the study (contracts, training, site set-up).

OVERALL 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 cost. 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-CI teams will have to justify the time they think is needed.

KCE has populated the grid with roles 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 e.g. a Chief Investigator should delegate all activities that can reasonably be delegated.

The number of suggested hours for each task are real life estimates and should be sufficient to cover the task. In case of deviations, this should be justified by the candidate Belgian Coordinating Site.

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. for the adaptation of the Patient Information and Consent Sheet, the Chief Investigator, Project Manager and Clinical Trial Assistant can all be involved. The total estimate of the time and costs related to this have been integrated into a fixed amount.

Depending on the study setting (hospital based, GP practices, …) 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.

The support that is received by the international sponsor should where applicable be added under each section. A grey shaded row has been introduced on the first line the different sections

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.
The first part of this section is calculated based on a fixed amount and includes the following:

- Adapt the protocol to the European/Belgian situation if needed
- Adapt documents for patients according to requirements in Belgium (e.g. Patient Information Sheet and Consent Form, specific questionnaires, …)
- Development of agreements with funder, vendor/contractors. KCE has templates that can be used.
- Costs for review of documents.
- Costs for translation of documents
- Initial selection of participating sites

The feasibility of the study depends on the number of sites to be visited. In the current pre-populated grid, 50% of the sites are scheduled to have an on-site feasibility visit and 50% of sites are scheduled to have a remote feasibility visit. For large scale trials (e.g. more than 50 sites), KCE suggests an on site visit in 10% of

the sites and remote feasibility check in the remaining 90% of the sites (250€/site). A minimum of 3 to 4 on site feasibility visits may however be needed, especially if the type of research is new for the site.
The conduct of the feasibility and site selection visits is the responsibility of the sponsor. In addition, KCE Trials will ask a contract research organisation (CRO) to complete an additional check of recruitment feasibility. Where appropriate, the sponsor feasibility visit and the CRO visit to the site can be combined.
The conduct of the feasibility and site selection visits is the responsibility of the sponsor. The BCC will assist in this for Belgian sites. Tasks related to the feasibility for Belgian sites should be detailed. In addition, KCE Trials may ask a contract research organisation (CRO) to complete an additional check of recruitment feasibility. Where appropriate, the sponsor feasibility visit and the CRO visit to the site can be combined.

The development of agreements with sites will depend on the number of sites involved. KCE templates can be used. In case GPs are involved or in situations where there is no negotiation with hospital direction required, the fixed amount for the contract development and negotiation needs to be reduced.

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
- The logistic activities for the submission of the dossier to the Ethics Committee(s)
- The logistic activities for the submission of the dossier to Competent Authorities, if applicable
- Provision of insurance, according to the legislation

As soon as the EU Regulation is implemented, this section will need to be adapted. Please contact KCE Trials if this is the case for your trial.

3. Monitoring

The purpose of trial monitoring is to verify that

- The rights and well-being of human subjects are protected
- The reported trial data are accurate, complete, and verifiable from source documents
- The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirements

Source: ICH-GCP E6 (R2) 5.18

This section should include the cost for the monitoring of the trial as specified above 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. It is important to develop a monitoring plan as soon as possible to determine the monitoring requirements and frequencies for the specific trial.

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:

- **Pre-study visit** (if applicable e.g. in case not all questions were covered during the feasibility or the feasibility was done remotely)
- **Training of CRAs**: this is the time needed for the CRAs to study the protocol and to 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 visited at a GP practice will be considerably lower than a trial which involves different hospital departments, pharmacy, lab etc. The suggested standard time for studies with GPs is 8 hours. The formula can be adapted as such and a comment should be added in the comments field. The suggested time includes the time to prepare, conduct and follow-up the visit and also includes the travel time to the site as well as the cost for travelling.

- **Conduct of on-site monitoring visits**: The suggested time (16 hours) needs to be adapted for studies with GPs (suggested time for studies with GPs is 8 hours). The suggested time includes the time to prepare, conduct and follow-up the visit and also includes the travel time to the site as well as the cost for travelling.
- **Conduct of study closure**: The suggested time (16 hours) needs to be adapted for studies with GP's (suggested time for studies with GP's is 8 hours). The suggested time includes the time to prepare, conduct and follow-up the visit and also includes the travel time to the site as well as the cost for travelling.
- **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, number of data points. The formula should be adapted depending on monitoring plan and a comment should be added in the comments field to justify the change.– This activity can be split between data manager or CRA.

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

The collection and maintenance of essential documents for management of the study is a sponsor responsibility. It can however be (partially) outsourced to the BCC. In that case the text below applies:

- This section includes all administrative activities related to the documentation, collection and archiving of essential documents for the sites and tasks where the BCC is responsible for: set-up and maintenance of a (e)TMF, (e)ISF, set-up and maintenance of a study portal
- This section includes the administrative work involved in the set-up, execution and follow-up of invoices and payments by the sponsor. Prior to the invitation to invoice, the amounts should be confirmed by data manager, CRA and project manager
- 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.
- Archiving: fixed amount of €250 per large box, assuming 2 boxes for the whole trial and 1 box for every 4 sites for 25 yrs archiving.
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6. Safety

The safety management of a study is a sponsor responsibility. It should not be taken care of by the BCC. Should any activities related to Safety Management be outsourced to the BCC, it should be captured here.

7. Data Management

Costs for this section should be covered by international sponsor.
Should any activities related to Safety Management be outsourced to the BCC, it should be captured here.

8. Statistics, report and publication

Costs for this section should be covered by international sponsor..

9. Project Management

This section consists of the project management activities for the Belgian sites and that are not mentioned in any of the above sections. It takes into account 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 above 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
    - As an example, time needed for day to day follow-up for a study with 10 sites and 100 patients in continuous follow-up for 1 years is estimated as 0,1 (=160h) FTE. This example can't be considered as applicable to every trial and needs to be adapted (but not multiplied) in case of more/less sites or patients - general project management should be taken care of by the sponsor.
- Project Status Reports (update KCE)
- Investigator Meeting(s) if applicable and not organised by the sponsor – attendance this meetings can be included as a cost here (attendance on an hourly fee basis)
- Steering Committee Meeting(s) if applicable and not organised by the sponsor – attendance this meetings can be included as a cost here (attendance on an hourly fee basis)

10. IMP/Intervention Handling

If the IMP is sourced by the international sponsor, this section should not be completed. If the BCC is responsible for purchasing, labelling, developing, tracking, etc of the IMP, the cost for this can be included here As KCE trials are pragmatic trials, efforts should be made to prescribe and invoice medication or other interventions as in routine practice.

- Sourcing of IMP, comparator/placebo, device, … (including import license if applicable)
- IMP or intervention accountability, will vary for pragmatic trials
- Packaging, blinding, labelling
- Storage, distribution, maintenance
- IMP destruction & recovery unused products

11. Overview of Site Costs

To report site costs, you have 2 possibilities

1/ Report site costs in the overall costs (line….) – with an automated formulae (2 hours per visit for study nurse and 10 minutes per visit for PI). The automatic calculation in this 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 as close to Standard of Care as possible.

Or

2/ Report site costs in the separate tab and include all procedures per protocol (see below)

In case the study requires non-standard of care visits and/or procedure/investigations, it is advised to detail the site costs in the separate tab detailing the costs according to the activities required by the protocol. Start-up costs for sites are taken from the budget parameters tab.
The overhead and margin can be added to site costs and should be paid to the sites.

A separate line in foreseen to cover the time for the use of EDGE, a web-based software tool in order to allow each participating site and KCE to monitor the recruitment at the participating sites in an anonymized manner "in real time". KCE will provide the tool free of charge. A flat fee of €25 (excl VAT but including margine and overhead) per patient for the recording of enrolment, randomization and completion in the EDGE tool within 5 working days of the respective visit is budgeted on top of the normal patient fee.

If the costs are detailed in the separate tab 'site costs', the automatic calculation in the tab 'overall costs' should be deleted. Otherwise, site costs are counted twice.

12. 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, …)
It is highly recommended to provide supporting information such as quotes (preferably from different providers) to support the amounts in this section. Candidate sponsors should check institutional procedures and regulatory requirements related to the need for (public) tendering.
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.
In general, no overhead or margin can be applied on these costs.

🗀 SITE COSTS (details)

In this tab an overview of protocol specific tasks should be generated. All activities that are considered as Standard of Care cannot be charged to the study budget. As KCE 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 need to be included here.

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