Manual
TBM Programme
"Applied Biomedical Research with a Primary Societal Finality"

Call 2024

Drafting and submission of a project application:

see website and e-portal!

see:

- http://www.fwo.be/en/fellowships-funding/research-projects/tbm-projects/
- https://fwoweb.fwo.be/

Basic objectives of the TBM programme

In the long term, the TBM programme aims at contributing to the implementation of (new) therapies, diagnostic techniques and preventive methods, which, without this government funding, would not make it to the patient due to a lack of industrial interest.

A TBM project meets the following criteria:

1. A TBM project aims at the development of a new **therapy, diagnosis and/or specific prevention of a particular human disease or medical issue** or **a comparison of existing therapies, diagnostics or preventive methods in order to find out their relative efficacy and cost-effectiveness**.
2. A TBM project is directed at **research** that is positioned **late in the path** from discovery to a specific application (i.e. there is a clinically relevant proof of concept) and aims at **translating** and developing scientific findings into clinical applications rather than creating knowledge *from scratch*. On the other hand, it is not positioned too late in the path from discovery to application: it does not consist of implementation activities that no longer require any research.
3. A TBM project offers a clear applicability with an **added value** for the **Flemish health situation**, including at least a **positive medical impact** for a particular group of patients or a **cost reduction for the Flemish healthcare system**.
4. At the time of submitting the application (or in the near future), the **industry is not interested** in the TBM project for commercial reasons.

Main programme characteristics

- A project application can be submitted by all Flemish research centres. Based on their mission, this includes e.g., **universities, university hospitals, university colleges (in Dutch: *hogescholen*)** and **strategic research centres**. Companies may not apply.
- A consortium of applicants or a single applicant can submit an application. Given the clinical focus of the programme, the consortium of applicants must however include at least **one Flemish hospital** (or ITM) for at least 10% of the total budget[1].
- The project budget ranges between 215,000 euro and **850,000** euro and the project duration ranges from **2 to 4 years.** The support percentage is 100% of the accepted projects costs. Exceptionally, a budget up to 1,275,000 euro is allowed for large scale and/or multicentre trials, given a thorough motivation.
- It is highly recommended to set up an **advisory committee** during the preparation of a TBM project. This committee consists of societal stakeholders (such as patient organisations) who will later be involved in the further utilisation path. By actively involving these stakeholders in an early stage of the project preparation, the research approach and the utilisation path can be optimised to increase the likelihood of an effective and broad implementation of the TBM project results in clinical practice.

Important data and available budget: see website

Document summary (see http://www.fwo.be/en/fellowships-funding/research-projects/tbm-projects/)

- TBM manual (this document)
- Cost model
- TBM scoring grid **NEW!**
- TBM template declaration of intent
- Regulations TBM programme: applies to all phases of the evaluation and execution of the project

[1] The ITM enjoys a special status in that it can submit a TBM project without the presence of a Flemish hospital.

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1. POSITIONING

1.1. Key characteristics of the TBM programme

On 15 September 2006 the Flemish government approved the legal decision[2] which establishes the framework for the project-based financing of "Applied Biomedical Research with a Primary Societal Goal" within the TBM programme.

The TBM programme targets a particular niche within biomedical research: advanced ("late stage") application-driven (bio)medical research with a marked societal applicability, yet with only limited industrial interest. Possible causes for the limited industrial interest include for instance difficult patentability, small patient populations, very low profit margins or patient-specific treatments which do not allow for the sale of a standardised product. When the industry is interested in the project results, but refuses to invest in the product/service because of e.g., the economic crisis, the project is ineligible for support under the TBM programme.

This particular focus of the TBM programme is mainly due to the observation that the funding possibilities for this type of research are very limited (as the industry is not interested and the government subsidy channels are mainly aimed at fundamental & basic research on the one hand and applied research with an industrial finality on the other hand). As a result, potential new treatments or diagnostics do not make it to the patient. By financing this type of research the TBM programme wants to contribute in the long term to the implementation of new therapies and diagnostic techniques, and thus aims at improving patient well-being and public health in general.

The above implies that projects can only qualify for a grant under the TBM programme if **each** of the following conditions is met:

1. The project consists of biomedical research with the aim of contributing to the development of a **new therapy, diagnosis and/or specific prevention of a particular human disease or medical issue** or **a comparison of existing therapies, diagnostics or preventive methods in order to find out their relative efficacy and cost-effectiveness.**
2. The research is positioned **late in the path** from discovery to a specific application and aims at **translating** and developing scientific findings into clinical applications rather than knowledge creation *from scratch*. Research at an early(ier) stage of the process can be submitted in the Strategic Basic Research (SBO) programme of FWO (see also 1.2 Positioning with respect to the SBO programme). On the other hand, it is not positioned too late in the path from discovery to application: it does not consist of implementation activities that no longer require any research.
3. The research has a clear applicability that offers an **added value** for the **Flemish health situation**, including at least a **positive medical impact** for a particular group of patients or a **cost reduction for the healthcare system**.
4. At the time of submitting the application (or in the near future), the **industry is not interested** in the project due to commercial reasons.

An overview of supported projects since 2016 can be found on the FWO website: https://www.fwo.be/en/news/results/research-projects-and-research-grants/. An abstract of each project can be consulted via the FWO database for financed research: https://www.fwo.be/en/financed-research/database-financed-research/. This overview can give an indication of whether your own project idea potentially fits the programme. However, all researchers are strongly advised to consult the FWO regarding new project proposals (see Chapter 5: ADDITIONAL INFORMATION).

[2] Decree of the Flemish Government for the funding of applied biomedical research with a primary societal finality, published in the Belgian Official Journal on 28/11/2006.

1.2. Positioning with respect to the SBO programme

- The SBO-M programme (Strategic Basic Research with a Societal Goal; 100% grant) comes closest to the TBM programme. It is directed at strategic basic research (*early stage*) at the research centres, with a marked societal applicability. Compared with the TBM programme, projects submitted under the SBO programme are at an earlier stage in the path from discovery towards a specific application and therefore place greater emphasis on knowledge acquisition. Moreover, SBO-M projects must meet higher requirements in terms of challenging character and innovativeness.
- The SBO-E programme (Strategic Basic Research with an Economic Goal; 100% grant) is directed, just like the SBO-M programme, at the early stage of strategic research at the research centres, but focuses on projects with an economic/industrial applicability. In addition to the differences with the SBO-M programme that were already mentioned in the previous paragraph, the SBO-E programme thus differentiates itself also from the TBM programme by its focus on industrial applicability. It should be noted here that projects that have so far not attracted any interest from industry because they are still at an early stage (e.g., no proof of concept), belong to the SBO-E programme and not to the TBM programme!

2. PROGRAMME CHARACTERISTICS

2.1. Project consortium and stakeholders

2.1.1. Main applicant and possible co-applicant(s)

An applicant is defined at the level of the legal entity, not at the level of a department or research group.

Any **Flemish research centre** can submit a TBM proposal. Based on their mission, this includes e.g., Flemish universities and their university hospitals, Flemish university colleges (in Dutch: *hogescholen*)[3] and the Flemish strategic research centres. Otherwise, all other organizations that meet the definition of a research centre (see box below) and that are located in the Flemish region[4] may act as applicants of a TBM project. For-profit actors (e.g., companies) cannot act as applicant or co-applicant of a TBM proposal. An overview of the type of organisations that are currently considered as research centres can be found in Annex I. If you have questions whether your organization is considered as a research centre, you can contact FWO via tbm@fwo.be.

> *A research centre is defined as an entity (such as universities or research institutes, technology transfer agencies, innovation intermediaries, research-oriented physical or virtual collaborative entities), irrespective of its legal status (organised under public or private law) or way of financing, whose primary goal is to independently conduct fundamental research, industrial research or experimental development or to widely disseminate the results of such activities by way of teaching, publication or knowledge transfer. Where such entity also pursues economic activities the financing, the costs and the revenues of those economic activities must be accounted for separately. Undertakings that can exert a decisive influence upon such an entity, in the quality of, for example, shareholders or members, may not enjoy preferential access to the results generated by it. (definition of a 'research and knowledge-dissemination organisation' as stated in Article 2, section 83 of the Regulation (EU) No 651/2014 of the commission of June 17, 2014).*

[3] See article II.2 en II.3 in: http://data-onderwijs.vlaanderen.be/edulex/document.aspx?docid=14650.
[4] Or in the Brussels region if they resort under the authority of the "Vlaamse Gemeenschapscommissie".

A consortium of applicants (with one main applicant and one or more co-applicants) or a single (main) applicant can submit an application. Given the clinical focus of the programme, however, at least one **Flemish hospital** (or ITM[5]) must be included in the consortium of applicants.

The main applicant appoints a **supervisor**. The supervisor must be employed by the main applicant and is responsible for the proper execution of the project. The supervisor is the first contact person for FWO. The main applicant ensures that the supervisor has sufficient time and experience to carry out this assignment properly.

If the project is submitted by a project consortium, the main applicant represents the applicants towards FWO and, when the grant is awarded, ensures the coordination of the activities of the awarded project grant.

All applicants must subscribe to the principles of the TBM programme in the form of a declaration of intent. This declaration also contains a formal statement in which the applicant declares that the organisation fulfils the definition of a research centre (see above). For applicants that regularly submit TBM project proposals[6], the research coordination or TTO offices have (or will receive upon request) an account to the "back office module" of the e-portal, allowing them to submit this declaration by simply agreeing with the conditions in the e-portal. For other non-regular applicants (such as non-Flemish research institutes, …), the declarations have to be uploaded as attachments to the project application at the time of submitting the proposal via the e-portal. A template is available on the website.

If the project is approved, all applicants will conclude a mutual agreement governing the practical cooperation, as well as the mutual agreements concerning the ownership and validation of the research results (see also: Chapter 4: RIGHTS AND OBLIGATIONS).

2.1.2. Non-Flemish co-applicants

Non-Flemish research centres can be included in the consortium as co-applicants. A condition is, however, that the total budget for non-Flemish research centres does not exceed **20%** of the total budget.

2.1.3. Subcontractors

In a project, the implementation of specific operational subtasks can also be entrusted to **subcontractors, including companies**. These will always be routine tasks, such as the inclusion of patients, without any creative input. The cumulated contribution of subcontractors must however not exceed **50%** of the total budget.

2.1.4. Broad target group for the project results

The end target group of the project is a particular group of patients. The project must be able to bring added value to this group of patients. An important aspect here is that the project attempts to reach the complete patient group that could be able to benefit from the project.

The project must provide for broad knowledge dissemination throughout the European Union through the utilisation activities. The dissemination and utilisation should be non-discriminatory in nature. The research findings must be easily accessible to the broader target group.

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[5] The Institute for Tropical Medicine (ITM) enjoys a special status in that it can submit a TBM project without the presence of a Flemish hospital.

[6] KU Leuven (incl. University Hospital Leuven), Ghent University, University Hospital Ghent, University of Antwerp, University Hospital Antwerp, Free University of Brussels (incl. University Hospital Brussels), University of Hasselt, Flanders Institute for Biotechnology, Prince Leopold Institute of Tropical Medicine.

When a project includes the development and/or validation of a software application, the applicants must specify a proposed software exploitation route. After completion of the project, the software should be exploited as open source software.

2.1.5. Advisory committee

For each TBM project, it is highly recommended to set up an **advisory committee**, at the start of the project preparation phase, consisting of parties that will be involved in the further utilisation process.

The active involvement of such an advisory committee in the various project phases (preparation, project implementation, post project activities) will stimulate both the effective implementation and the dissemination of the TBM project results from the outset of the project. The applicant is encouraged and stimulated to build a network with important players in the further utilisation trajectory, so that the transfer of project results is (better) supported and broadened.

The assessment of TBM projects will explicitly take into account the composition of the advisory committee and the commitment of its members to contribute to the further utilisation process.

The role of an advisory committee is to support the translation of project results towards the clinical application (both from the regulatory framework and from the patient's point of view/demand side) on the one hand, and active involvement in implementation and dissemination of project results on the other hand (e.g., advice on feasibility of the utilisation during the project). During the project preparation, a two-way dialogue is expected with the applicant (identify practice needs/bottlenecks, discuss the project approach, assist in designing and preparing the translation to clinical practice, options for reimbursement, etc.). During the project, the committee monitors the project results and provides input to resolve potential problems (e.g., change of protocol, assist with inclusion problems, etc.). The ultimate goal is to generate a bigger impact through the TBM project.

The societal stakeholders involved are specific to each TBM project. Possible members of an advisory committee include patient organisations, professional associations, regulatory agencies or advisors, health insurance organisations, hospitals/research centres/genetic centres/homes for elderly and nursing homes that wish to implement the results, clinical partners that provide access to patients, statistical centres, tech transfer organisations, or possibly a company (e.g., a contract manufacturing organisation) that will produce the end product of the TBM project (without interest to develop the product internally, see criterion "lack of industrial interest"). Foreign organisations are allowed in the advisory committee. An evaluation of completed TBM projects showed that reimbursement is often one of the bottlenecks for broad utilisation of the results. Applicants are therefore strongly advised to engage in early interaction with relevant stakeholders (e.g., RIZIV-INAMI) to overcome this potential hurdle.

Although all possible stakeholders should be well represented in the advisory committee, the involvement of patient organisations will receive special attention during the evaluation. Ideally, patient organisations have been consulted while developing the proposal, and their impact on the design of the study should be described in the proposal. Also, how patients will be involved during and after the project should be demonstrated.

When installing an advisory committee, the applicant should:

1. Compose this committee depending on the needs and relevance for the TBM project (not limited to members of the research consortium).
2. Initiate **early and meaningful interactions** with the members of the advisory committee during the project definition and development.
3. Add a motivated letter of intent for each member of the advisory committee by the deadline for submission of the application. It is essential that the letters of intent indicate the added value of each member of the advisory committee and do not remain limited to general non-binding expressions of interest. In the case of an organisation: each letter needs to be signed by a legal

representative of the organisation (as evidence of the support within the organisation), otherwise the letter will not be taken into account.

4. Specify in the proposal which interactions already took place with the members of the advisory committee prior to submission of the proposal (preparatory phase), what the impact of the interactions was on the project, what the added value is of the different committee members and what their final role will be in the utilisation or post-project phase.
5. Foresee a minimal interaction frequency of **once a year** during the project (follow-up meeting), invite the FWO to this meeting and send the minutes of the meeting to the FWO.

2.2. Supported activities

The TBM programme is explicitly targeted at **research** that meets **each** of the four criteria that you can find below. A list of previously funded projects is available on our website: https://www.fwo.be/en/news/results/research-projects-and-research-grants/. More information on these projects can be found on the FRIS research portal: https://researchportal.be/en/.

1. The project consists of biomedical research with the aim of contributing to the development of a new **therapy, diagnosis and/or specific prevention of a particular human disease or medical issue** or **a comparison of existing therapies, diagnostics or preventive methods in order to find out their relative efficacy and cost-effectiveness.**
   Examples of research that does NOT fit within the scope of the TBM programme include:
   - Research that is not (bio)medical in nature, i.e. research that cannot contribute to a better insight into the root of human disease and health;
   - Assessments of health organisations;
   - Epidemiological studies;
   - Research that is aimed at a general improvement of health (e.g., general prevention, general nutrition advice or general exercise advice);
   - Introduction into Flanders of a therapy or diagnosis used abroad.
2. The research is positioned **late in the path** from discovery to a specific application. It is focused on research in patients for which a good feasibility of the clinical application aimed for can be motivated based on clear and concrete data and arguments that substantiate an acceptable safety and efficacy of the targeted clinical application ("proof of concept"). These arguments can e.g., result from data in the targeted patient group (a limited group of patients or case studies), from data in a comparable group of patients or from data in an animal model with demonstrated clinical relevance. The data may have been obtained by the applicants themselves or by other research groups. The research is aimed at **translating** and developing a scientific finding into a clinical application rather than knowledge creation *from scratch*. It is focused on the *validation* of findings in a (larger) group of patients, not on the *identification* of new biomarkers, therapies, algorithms or care paths.

   In general, a research proposal could fit the TBM programme if sufficient evidence exists that a technology can be effective. A typical funded TBM study usually determines effectiveness by testing for a clinically important difference in a relevant primary outcome measure. The TBM evaluators needs to be convinced that the primary outcome effect that the trial or study is powered to detect is plausible in the light of knowledge of how the intervention works and existing evidence. An application should contain a clear explanation of how the intervention works and how it can produce the clinically important difference in the primary outcome. Examples of proof of concept that could be accepted for the TBM programme can be found at similar funding schemes abroad, e.g. https://www.nihr.ac.uk/documents/proof-of-concept/19909.

   Health economics studies that are aimed at measuring the benefit of the new therapy/diagnostic/preventive method for the health care system can be part of the TBM-project.

On the other hand, the project is not positioned too late in the path from discovery to application: it does not consist of implementation activities or engineering activities that no longer involve any research. In practice, this means the following:

- If certain routine (or implementation or engineering) activities (such as the production of a protein, the construction of a demo, the training of employees, etc.) are necessary to be able to perform the subsequent **research** in the TBM project, such activities can be accepted as part of a TBM project so long as they do not take the upper hand in the project.
- If, by contrast, certain routine activities (or implementation or engineering activities) are not necessary for the execution of the research and are to be regarded primarily as side line or post-research activities, such activities cannot be accepted as part of a TBM project.

Examples of research that does NOT fit within the scope of the TBM programme include:

- Implementation of acquired knowledge from the past (e.g., drafting of SOPs, provision of training, etc.) without the need for further research in the process;
- Market research for utilisation of the project findings;
- Fundamental research that is mainly directed at knowledge creation *from scratch*;
- Basic research that builds on previously acquired knowledge, but that is still far from clinical applicability (no proof of concept reached as yet): e.g., identification of new biomarkers, development of a new algorithm;
- Translational or clinical research for which the proof of concept is limited, for example because (i) the efficacy of the application has not been demonstrated in large-animal-studies, case studies or studies with a limited number of patients or (ii) the cumulative clinical literature concerning the application is insufficient;
- Research aimed at improving the care path of a specific disease for which a proof of concept is available for the therapy itself but not for the innovation concerning the care path.

Note: Concerning the **advisory committee**, no TBM financing is foreseen for the implementation of the **pre-project phase** - prior to the project execution - or for the participation of an organisation in the advisory committee. Activities during the project execution that are linked to utilisation afterwards (such as meetings with the advisory committee) can be taken into account for support so long as their share is limited. When, upon completion of a successful TBM project, the focus shifts towards the organisations from the work field involved, the further implementation (incl. dissemination) of the TBM project results (**post-project phase**) does not fall within the TBM financing channel. It is important to clearly indicate in the utilisation plan which additional steps are needed with regard to the implementation after the TBM project has ended. Describe which actions will be undertaken by various stakeholders for a successful implementation (stakeholders should include concrete commitments in their letter of intent).

3. The research has a clear applicability that offers an **added value** for the **Flemish health situation**, including at least a **positive medical impact** for a certain group of patients or a **cost reduction for the Flemish healthcare system**. When the research is not aimed at a positive medical impact but merely involves a cost reduction for the Flemish health care system, then this cost reduction should be substantiated by a preliminary health economic analysis/argumentation.
4. At the time of submitting the application (or in the near future) there is **no industrial interest** in the project, nor is there any reason for the existence of a potential spin-off. Possible reasons for the lack of industrial interest in a late stage project (where proof of concept has already been reached) with an added value for health, may include the following:
    - Lack of patentability;

- Small patient populations, so that the return on investment is too small for pharmaceutical companies (e.g., certain cancers affecting children);
- High costs of individual treatment that squeeze profit margins (e.g., autologous cell therapy, tissue engineering);
- High commercial risk (e.g. xenotransplant);
- Insufficient profit margins;
- The absence of legal obligation for the producer of a medical application (e.g., a medical device) to test its efficacy. Hence, it is allowed to submit proposals directed towards the evaluation of the efficacy, safety and cost-effectiveness of a medical device that is marketed by a company. Important to note is the fact that this study should be conducted independently from the company. This independence must be clearly substantiated in the project application (both by a formal declaration of the applicants and a short motivation). In publications, resulting from the study, the independence should also be mentioned.

Examples of research that does NOT fit within the scope of the TBM programme include:

- Research aimed at a specific company. Such research can be supported in the R&D programme of the Agency for Innovation and Entrepreneurship;
- Research for which industrial financing can reasonably be expected today, be it in Flanders or abroad;
- Research for which industrial interest can reasonably be expected today, but in which the industry is reluctant to invest because of the economic crisis;
- Research which the applicants do not wish to transfer to the companies as yet, in order to be able to extract better conditions from the companies at a later stage;
- Research for which the lack of industrial interest is above all the consequence of a high scientific risk (projects positioned too early in the path from discovery to application) or of an insufficient project quality;
- Research for which no spin-off can be established yet because of too high a scientific risk or because of the lack of financial resources;
- Research aimed at the evaluation of a medical device in collaboration with a company.

Note: This condition does not exclude those projects in which the industry, despite the current lack of interest in participating in the project (e.g., due to too low a profit in proportion to the R&D costs), becomes involved at a later stage, notably in the utilisation of the results (and from which it derives a limited benefit) for example through production or distribution activities.

As already stated above, projects designed to compare the efficacy of a medical device with the gold standard, may fit within the TBM programme. Such projects should be done by a completely independent party. In that case the applicant shall provide a sworn statement to FWO and shall state independence in any publication concerning the project results.

2.3. Project budget and financing

2.3.1. Project budget

A TBM project will last a minimum of 2 years and a maximum of 4 years. The project budget must range between 215,000 euro and 850,000 euro. In exceptional cases a budget up to 1,275,000 euro is allowed for large scale and/or multicentre trials. In this case, the higher budget has to be substantiated extensively! The necessity for the higher budget will be evaluated explicitly by the expert panel.

An Excel template for preparation of the budget is available on the FWO e-portal. This file makes use of macros to facilitate its completion. Its use is mandatory and has to be uploaded in the FWO e-portal when submitting the project proposal. *Please note:* Before uploading this file to the FWO e-portal, you need to save this document as an Excel file without macros (extension xls(x) instead of xlsm).

The rules to be followed for drafting the project budget are set out in the **cost model**, which is available on the FWO website (http://www.fwo.be/en/fellowships-funding/research-projects/tbm-projects/). All acceptable costs are real costs that can be justified. Briefly summarised, the TBM budget is based on the following principles:

If a project application is submitted by a consortium of applicants, a sub-budget is prepared for each applicant (at legal entity level)[7]. Together, the different sub-budgets make up the project budget.

The acceptable staffing costs form the basis of each sub-budget. Only staff members who carry out research activities or utilisation preparing activities for the project can be included in the project budget.

The other costs (consumables and equipment) must be real costs and related to the project.

The costs of large, specific subcontracting contracts should be included in the consumables section.

For TBM projects, it is also required that:

- the aggregated share of the applicants that are Flemish hospitals or ITM amounts to at least **10%** of the total project costs (cf. eligibility criteria). This can be verified by FWO at the time of the final financial settlement.
- the total budget for non-Flemish research centres does not exceed **20%** of the total budget.
- the cumulated contribution by subcontractors is limited to **50%** of the total budget.

The project period (2-4 years) cannot be prolonged, but expenses (staffing, consumables and equipment) are accepted if they are dated during the project duration plus the following two years.

2.3.2. Grant

The **grant** for TBM projects amounts to **100%** of the acceptable costs.

Attention: Although it is required that the Flemish hospitals should have a cumulated minimum share of 10% in the total project budget, this does not mean that the Flemish hospitals must finance this share themselves!

3. EVALUATION OF A PROJECT APPLICATION

3.1. Timing

Each year a call is issued on the FWO website in which the time lines for evaluation of the proposal are indicated. Project proposals need to be submitted via the e-portal of FWO (https://fwoweb.fwo.be/).

3.2. Eligibility

After the submission, FWO assesses whether the project applications are formally eligible based on the following criteria:

[7] In a project where a Flemish university and its university hospital (with a separate legal entity) are both members of the project consortium, one overall budget may be submitted for both entities. Both the university and the university hospital should still identify themselves as individual applicant in the project proposal to make it clear that both entities are to be included as contractor in the contract. It should also be demonstrated that the aggregated share of the Flemish hospitals (or ITM) amounts to at least 10% of the total project costs (cf. eligibility criteria).
For the final financial settlement, the Flemish university and its university hospital can be considered one virtual entity. This means that budget shifts between both entities are possible. The budget shifts must remain in line with the initial innovation goal and the aggregated share of the Flemish hospitals (or ITM) should not fall below 10% of the total project costs.
If a university and its hospital wish to be regarded as one single virtual entity, they have to submit a written declaration to FWO (signed by both legal representatives). The declaration could refer to their total TBM portfolio (thus agreeing, for the total TBM portfolio, with budget shifts between the university and its hospital within a particular project). Alternatively, the declaration may be project specific.

1. The project application was submitted (by the main host institution) via the FWO e-portal and was received by the set deadline as specified on the TBM website;
2. The project application was prepared in accordance with the information requested in the FWO e-portal;
3. All applicants of the consortium have subscribed to the principles of the TBM programme in the form of a declaration of intent;
4. Each applicant of the consortium meets the definition of a "research centre" (see 2.1.1).
5. The consortium of applicants contains at least one Flemish hospital (or ITM) whereby the cumulated share of Flemish hospitals (and ITM) account to at least 10% of the total project budget[8];
6. The project application includes a research proposal that positions itself within the objective of the call (see 4 conditions in 1.1);
7. The project application is written in English to allow for its assessment by (inter)national experts;
8. The project application includes a project budget prepared in accordance with the cost model.

The FWO board of trustees will approve the (in)eligibility of the applications. If a project application is considered ineligible, the main applicant will be notified thereof as soon as possible. Projects that are found to be ineligible will not be considered in the further assessment and selection procedure. The eligibility criteria remain valid throughout the evaluation procedure.

FWO may contact the applicant during the eligibility analysis to complete the application. FWO may also use information from other financing bodies.

3.3. Assessment

3.3.1. Assessment procedure

First, the application is evaluated in writing by members of the TBM expert panels and (inter)national reviewers with expertise in the specific research domain of the proposed project, see also Regulations FWO - internal and external peer review. Experts who are involved in (at least) one of the project proposals are excluded from participating in the expert panels. Furthermore, experts who are not involved, but who are affiliated with a division/service/department identical to that of one of the applicants, **may not take part** in the assessment of the corresponding proposal.

The written reviews are then sent to the applicants, who have the opportunity to rebut factual errors or provide additional clarification to the reviewers. In the rebuttal phase, it is not allowed to provide new data or change the original concept or methodology of the proposed study.

Subsequently, another TBM panel member appointed as 'rapporteur' generates a synthesis of the proposal, the peer review reports and the rebuttal letter. Based on this information the rapporteur suggests a preliminary score for the proposal using the TBM scoring grid. The provisional scores and ranking are shared with the entire panel prior to the evaluation meeting. During this meeting, moderated by FWO staff, the panel members discuss the strengths and weaknesses of the applications to determine consensual scores and establish the final ranking. The assessment takes place based on quality criteria and on the fit of the projects within the TBM programme. Proposals are assessed according to internationally accepted standards[9].

In addition to a consensual score for the criteria, the panel also awards a general appreciation score (A, B, C) to the project proposal:

[8] This "10% rule" remains valid throughout the execution of the TBM projects. During the financial settlement upon completion of the project, FWO can verify whether the aggregated share of the Flemish hospitals (or ITM) amounts to at least 10% of the total project costs.

[9] In case it includes a clinical trial, please indicate in your application which reporting guideline will be followed.

- A: The application meets the minimum quality requirements and is eligible for support, provided sufficient budget is available. If ranked below the limits of the available budget, an A-type project can be resubmitted within the TBM programme in the next call.
- B: The application does not meet the minimum quality requirements and cannot be supported in its current form. Shortcomings in the current application are relatively easy to remedy. B-type projects may be resubmitted in the next call. At that occasion, the applicants must explain how the research and valorisation plan has been revised in order to meet the criticism of the previous call, with an emphasis on the criteria on which the score was substandard as listed in the feedback.
- C: Category C concerns applications that clearly do not meet the minimum quality requirements for support (e.g., the proposal does not fit the finality of the program, the project or parts thereof have been submitted too prematurely, a clearly negative appreciation on both assessment axes, particular negative appreciation of the scientific quality, shortcomings that are difficult to remedy within the timeframe of one year). In case an application is classified in category C, it cannot be resubmitted the next call. In other words, a call year must be skipped before a proposal with the same research questions and valorisation objectives can be submitted.

Applicants who received a C-score for an application can still submit a different project proposal (i.e. with entirely new scientific and utilisation objectives) within the next call. At all times, the evaluation bodies have the right to not evaluate an application and/or exclude it from the final ranking, if it is too similar in terms of scientific or utilization objective to a project with a C-score from the previous call. This assessment is part of the exclusive and discretionary competence of the evaluation body concerned.

Finally, based in part on the available information and the recommendation of the expert panels, the FWO board of trustees decides on whether or not to award the grant and on the scope and the nature thereof, as well as on the particular terms and conditions.

Irrespective of the assessment procedure, the board of trustees may make a negative decision or set additional conditions spurred by the failure to meet additional obligations or authorisations imposed by the authorities, or following incorrect behaviour during previous applications (concerning the provision of information, substantive and financial obligations or reporting).

Both the FWO staff, the external experts and the members of the FWO board of trustees undertake to treat the information on each project confidentially during the assessment process, and not to disclose any data to third parties or to apply it for their own benefit.

3.3.2. Assessment criteria

The projects are assessed from two main viewpoints (Scientific Quality and Societal Utilisation Perspectives), which both encompass several criteria. The two main viewpoints carry the same weight. In addition, the evaluators will specifically assess whether the proposal adheres to the four criteria of the TBM programme, see 'key features' under 1.1. Failure to adhere to any of the four criteria will automatically result in a critical score, which will prevent the proposal from receiving funding.

The criteria that will be assessed during the assessment committees are briefly discussed below:

Fit to the scope of the TBM programme

F1. Focus of the project on the development of a new therapy, diagnosis and/or specific prevention of a particular disease or medical issue or a comparison of existing therapies, diagnostics or preventive methods in order to find out their relative efficacy and cost-effectiveness *(pass/fail)*
Is the project aimed at (i) the development of a new therapy, diagnosis or specific prevention of a particular disease or medical issue or (ii) a comparison of existing therapies, diagnostics or preventive methods that provides information on their relative efficacy and cost-effectiveness? N.B. This criterion examines the objective in itself, rather than the approach.

F2. Positioning of the project in the path from discovery to application *(pass/fail)*
Does the project include research activities or are they purely implementation activities with only a very limited inherent risk? Is the research positioned late in the path from discovery to application and is it aimed primarily at translating a scientific finding into a concrete clinical application? Has a proof of concept already been obtained?

F3. Added value for the health situation in Flanders *(pass/fail)*
Is any positive impact anticipated either in view of the medical situation of the patient or in view of the Flemish society as a whole due to a reduced healthcare cost?

F4. Lack of industrial interest *(pass/fail)*
Can industrial interest already be anticipated for this project? Did the applicants provide convincing argumentation for the lack of industrial interest (due to a commercial reason)? Have the applicants actively questioned relevant industrial partners about their possible interest? N.B. If the expert panel has doubts about the industrial disinterest AND no convincing argumentation is presented in the proposal, a critical score will be appointed to this criterion. In this respect, written statements from relevant industrial companies in which they indicate that they are not interested in the project, may contribute to the argument that there is no industrial interest.

Scientific Quality

S1. Contribution to the international state-of-the-art *(10 points)*
Does the project make a contribution to the state-of-the-art in the targeted field or does it lags behind the current state-of-the-art in the field? What is the extent of the scientific importance of the objectives?

S2. Quality, relevance and feasibility of the research approach *(20 points)*
Is the proposed scientific approach suitable and efficient to reach the targeted scientific objectives? Is the research proposal statistically supported by a power analysis? Is allowance made for drop-outs? Is the proposed inclusion strategy feasible? A failing patient recruitment strategy often causes problems during the project. Therefore, during the assessment, special attention will be paid to the feasibility of the proposed inclusion strategy within the time frame of the project proposal. How is the balance between risks and feasibility? Does the project involve intrinsic scientific/technological risks? Are the applicants required to solve technological or scientific problems? What is the feasibility of the scientific project objectives? Are the applicants aware of the main risks and are "fall back scenarios" anticipated if necessary?

S3. Quality of project plan + management *(10 points)*
Is the work plan clearly defined, with well-defined and planned tasks that correspond to the project objectives? Are the different tasks/responsibilities shared clearly among the different research units, with a good estimation of the necessary person power per research unit? Are the major milestones and deliverables identified? Is the implementation of the proposed work programme feasible within the project duration? What is the cost efficiency of the project like?

S4. Competence and infrastructure *(5 points)*
Is all the necessary expertise and infrastructure present (or accessible) to implement the project correctly? Are all the skills brought together relevant for the implementation of the project? Is there an obvious synergy between the members of the consortium? Is there a significant cross-institutional cooperation?

Societal Utilisation Perspectives

U1. Relevance of the project in attaining the utilisation objective *(10 points)*
Is the research approach relevant and efficient to achieve the utilisation objectives? Are the set scientific objectives the most relevant to achieve the utilisation objectives?

U2. Quality and feasibility of the utilisation objectives and approach *(10 points)*

Is the targeted utilisation strategy adequate to translate the project results into the targeted utilisation objectives? What is the feasibility of this project in order to reach the targeted utilisation objective? The feasibility of the utilisation objectives may be dependent on various bottlenecks such as scientific issues during and after the project implementation, ethical objections, regulatory aspects, "freedom to operate", etc. Are the applicants aiming at the relevant target group(s)? Was a relevant advisory committee set up (including relevant patient organisations)? Do the applicants adequately use the expertise and commitment of the members of the advisory committee in order to achieve the proposed utilisation objectives? Are the applicants aware of possible bottlenecks in the transfer of the results to the patient and are there planning strategies to resolve this, if necessary? Will it be possible to reach a large part of the target group? Will the results be disseminated widely in the European Union, and on a non-discriminatory basis?

U3. Anticipated impact for the individual patient or cost reduction for Flemish healthcare *(20 points)*
What is the extent of the anticipated medical impact/added value of the project for the individual patient, taking into account the intrinsic feasibility of the targeted application? How many patients in Flanders will benefit from the results of this project, taking into account the intrinsic feasibility of the targeted application? What is the extent of the anticipated medical impact for these patients? Is the project expected to result in a significant cost reduction for the Flemish health care system (taking into account the intrinsic feasibility of the targeted application)?

U4. Competence and track record in terms of transfer and utilisation *(5 points)*
Do the applicants and the members of the advisory committee together have the necessary expertise/track record to take the project results to the targeted patient group (with as big a range as possible)? Have previous and/or ongoing TBM projects already led to a transfer?

3.3.3. After the decision

The project data sheet with the decision-making arguments is forwarded to the main applicant when the decision is made. The applicants can, at any time, request a debriefing from FWO (via tbm@fwo.be).

Where the decision is positive, an agreement is drawn up between FWO and the project applicants (see Chapter 4: RIGHTS AND OBLIGATIONS).

In the case of a negative decision, based on clear and verifiable elements a request for review of the decision can be filed with FWO. The appeal procedure is detailed on the website.

If dissatisfied with the way FWO has handled the application, a complaint can be filed at any time in writing or electronically.

4. RIGHTS AND OBLIGATIONS

4.1. Agreements

4.1.1. FWO agreement

In the case of a positive decision by the board of trustees, a grant agreement is drafted in which the contractual modalities of the project between FWO and the project applicants (beneficiary) are set forth. The agreement is drafted by FWO. Both the main applicant and the co-applicants must sign this agreement.

The main obligation of the beneficiary is a commitment of resources: with the help of the agreed resources, the beneficiary will make the necessary efforts to reach and apply the described project objectives through research and development activities to ensure utilisation in Flanders.

The agreement also contains a clause in which the beneficiary declares that animal experiments/patient studies/studies on patient material under the project will only be carried out as soon as all required approvals from the ethical committee(s) and/or regulatory agencies have been received.

4.1.2. Cooperation agreement

If there are several applicants, they must set up a mutual cooperation agreement. With a view to obtaining FWO's approval, this agreement should cover at least the following in sufficient detail:

- designation of the coordinating institution and a supervisor;
- designation of the services or products to be delivered;
- agreements as regards ownership and user rights to the project results;
- procedure for settlement of mutual disputes.

The cooperation agreement must concur with the FWO agreement, and in particular with the provisions regarding the utilisation of the project results. The beneficiary must forward the cooperation agreement to FWO within four months after the FWO agreement was sent by FWO.

4.2. Use of findings

4.2.1. Legal obligations and knowledge dissemination

The project consortium has the obligation to exploit the project findings as broadly as possible in order to achieve maximum added value for the targeted patient group. To that effect, the project consortium must, among other things, disseminate the project findings to a broad target group by organising knowledge dissemination activities.

4.2.2. Ownership of the findings

The project consortium of applicants is the owner of the research findings. Members of the advisory committee or subcontractors, whose contribution is by definition limited to the provision of goods or services, cannot claim any rights of ownership.

Where relevant, the project application should specify how IPR will be handled.

The project consortium draws up a cooperation agreement (following the financing commitment). This agreement governs the (joint) ownership of the project findings and the user rights to the background knowledge.

4.3. Monitoring and reporting

If the project is approved, the beneficiary will have to report at regular intervals on the proper implementation and progress of the project. This aspect is covered on the website.

4.4. Scientific standards

FWO requires that researchers adhere to the highest scientific standards and the regulations with respect to research integrity as formulated in Article 4 bis of the FWO General regulations. Moreover, to promote free access to scientific knowledge and cultural heritage, Article 2 of these regulations states that beneficiaries of an FWO project must deposit the publications that result from the subsidy in a public “Open Access” database, within one year from the date of publication, in order to effect greater impact and utilisation of their work. Researchers are also advised to publish their other publications in such an "Open Access" database, the so-called "Open Archives", together with the research data that resulted in these publications.

For clinical trials[10], FWO requests compliance with relevant **reporting guidelines** that have been developed to improve the design, analysis and reporting of experiments, such that readers can assess

[10] For this purposes, a clinical trial is seen as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials include interventions such as, but not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc. This definition includes Phase I to Phase IV trials.

the robustness of the findings and reproduce the work if they wish. For randomized clinical trials the CONSORT guidelines are endorsed. FWO requires that clinical trials are registered in a **recognised public clinical trial database** (e.g. https://www.clinicaltrials.gov), before the start of the trial. Once the first patient is recruited, the grant holder should inform FWO (via tbm@fwo.be) about the start date of the trial and the database registry number of the clinical trial.

All relevant fields and statuses in the registry must be updated on a regular basis throughout the duration of study and approved changes to the study protocol, etc., adjusted as appropriate and in line with instructions from the selected registry. Irrespective of the outcome of the trial, a sufficiently detailed clinical protocol, statistical analysis plan and summarised study results must be added within one year of the end of data collection.

Publishing in a (specialized) journal describing the design, the methods used and the results is a mandatory component of the project's activities. This also holds for projects that were terminated prematurely or that did not lead to the desired result. The clinical database concerned and identification code is to be included in all specialized publications on the clinical trial concerned in order to link scientific publications (with details regarding research methods and results) with the public registry's entry. Please note that FWO has an **Open Access publication policy**.

4.5. Data management

Research data management covers the way research data are managed, from their date of creation or collection, to the moment they are published or used and possibly preserved for the long term.

Research data management is therefore an integral part of sound scientific research and thus FWO has made data management a key element of its policy. It covers procedures on the description of research data and metadata, their storage and long-term preservation, the discoverability, the designation of responsible persons, the handling of highly sensitive data, and the open access to and sharing of research data. The FWO expects researchers to pay due attention to this dimension before, during and for at least five years following their research.

The application form in the FWO e-portal contains several issues that need to be addressed concerning data management:

- the data types that the research will use and/or generate
- the provisions that are in place in order to preserve the data for at least 5 years after the end of the research
- possible reasons to deviate from the principle of preservation of data, sharing and of the minimum preservation term of 5 years
- specific security measures for research data due to ethical issues
- other relevant issues related to data management.

The abovementioned issues regarding data management will also be taken into account during the evaluation procedure. If a proposal receives funding, a data management plan will be requested by the FWO. More information on data management can be found here.

5. ADDITIONAL INFORMATION

5.1. Abstract

All potential applicants are strongly advised to consult the FWO on whether a project idea may or may not fit within the programme objectives, by providing a short abstract (1-2 pages, sent via e-mail using the template available on the FWO-TBM website to tbm@fwo.be).

5.2. Preliminary discussion

Prior to preparing and submitting an application, an oral preliminary discussion at FWO can be requested. Requests for preliminary discussion must be sent to tbm@fwo.be, with the subject line "request for preliminary discussion". Please attach an abstract of the project proposal (1-2 pages; use the template available on the FWO-TBM website), as well as any questions that you would like to see answered.

5.3. Contact

For questions with regard to the modalities of the TBM programme, please contact tbm@fwo.be. Questions regarding the functionality of the e-portal should be addressed to fwohelpdesk@fwo.be.

Annex I: types of organisations considered as research centres within the TBM programme

Below you can find an overview of the types of organizations that can be considered as research centres based on the definition of a 'research and knowledge-dissemination organisation' as stated in Article 2, section 83 of the Regulation (EU) No 651/2014 of the commission of June 17, 2014.

a) Universities, university colleges, based in Flanders or abroad
b) Scientific institutions and strategic research centres
c) University hospitals/medical centre (autonomous organization)
d) Non university hospitals with an academic character
e) Non university hospitals without an academic character

Categories a) to d) are accepted as a research centre on the basis of their mission. Organisations in category e) and other organizations need to submit a legal advice and substantiation why they meet the definition of a research centre to FWO.