

Federal Ministry of Education and Research

Innovative Toxicology for the Reduction of Animal Experimentation (e:ToP)

Guidelines for Organizations Seeking Funding for e:ToP Pilot Projects

1. Purpose of Funding, Legal Basis

1.1 Purpose of Funding

The Federal Ministry of Education and Research (BMBF) intends to consolidate Germany's internationally competitive position both in the development of alternative methods to animal experimentation and in systems biology by focusing national expertise and selectively supporting interdisciplinary pilot projects.

The discrepancy between increasingly strict requirements for the safety of consumers and employees, for example with respect to the handling of chemicals, and efforts to reduce the number of animal experiments has led to a conflict of objectives. Establishing new *in vitro* test methods to replace experiments on animals in the area of toxicology can contribute to a solution for this dilemma. With a combination of new research approaches from the areas of molecular biology, bioinformatics and systems biology, these new toxicological methods can be established in a more targeted and efficient manner. Methods for the analysis of the genome, the transcriptome, the proteome and the metabolome have been well established for some time. Initial steps towards the bioinformatic analysis, visualization and integration of measured data for these molecular levels across the borders of areas of study referred to as "omics" have already facilitated a more holistic view of living systems, and thus permit systems biology analyses to be carried out by means of predictive modelling. Established methods and infrastructures in the area of omics, bioinformatics and systems biology can also be used effectively in the investigation of toxicological processes. By identifying the molecular signatures of toxicological processes, it will be increasingly possible to selectively develop *in vitro* test methods to replace experimentation on living animals.

The measure "Innovative Toxicology for the Reduction of Animal Experimentation" is initially announced by BMBF for pilot projects in order to clarify whether and to what extent omics analyses, bioinformatics and systems biology can contribute to a better understanding of toxicological processes and ultimately to the development of new predictive *in vitro* test methods to replace animal experiments. These projects will serve as a scientific basis for the subsequent translation phase, which will build on the findings from the pilot phase.

BMBF expects to receive innovative project ideas that aim to process omics data from toxicological *in vitro* experiments with methods commonly used in the areas of bioinformatics and systems biology methods so as to identify the toxic effects of chemicals on a molecular level. Toxicologists, molecular biologists, bioinformaticians and representatives of other areas should contribute to interdisciplinary research approaches to reach this objective.

1.2 Legal Basis

Projects can be funded with grants in accordance with these guidelines, BMBF's standard terms and conditions for grants on an expenditure or cost basis, and the administrative regulations supplementing Articles 23 and 44 of the Federal Budget Code (BHO). Applicants have no legal right to receive funding. The funding agency will make a decision after duly assessing the circumstances within the framework of the available budget.

Research in accordance with these present guidelines meets the requirements of Commission Regulation (EC) No. 800/2008 of 6 August 2008 declaring certain categories of aid compatible with the common market in application of Articles 87 and 88 of the Treaty (General Block Exemption Regulation), published in the Official Journal of the European Union L 214/3 of 9 August 2008, p. 3, and is therefore compatible with the common market under Article 107(3) of the Treaty on the Functioning of the European Union and not subject to the notification requirement in accordance with Article 108(3) of said Treaty. Eligible projects as per these present guidelines come under aid for research, development and innovation in accordance with Article 1(1), point (g) of the General Block Exemption Regulation in case recipients of grants are commercial undertakings.

In accordance with Article 1(6), point (a) of the General Block Exemption Regulation, any undertaking which is subject to an outstanding recovery order following a previous Commission Decision declaring an aid illegal and incompatible with the common market shall not be eligible for individual aid.

More information on the Federal Government's Health Research Framework Programme, which falls under the General Block Exemption Regulation, can be found on the Internet at <http://www.gesundheitsforschung-bmf.de/media/Gesundheitsforschungsprogramm.pdf> (in German) or at <http://www.bmf.de/en/gesundheitsforschung.php>.

2. Projects to be Funded

Funding is available for innovative, application-oriented pilot projects of interdisciplinary research collaborations that aim to generate substantial scientific progress in the understanding of toxicological processes in the human body. Using established methods, researchers are to investigate in parallel the effects of chemical substances (as defined in the European chemicals directive REACH) on the transcriptome, the relevant proteome, the metabolome, and, if mutagenicity is possible, also on the genome. The metabolism should be one of the priorities in the functional analysis of integrated data. In the projects eligible for funding under these guidelines, it can be assumed that human cell lines or *in vitro* models of human tissue will be used. As part of the projects, molecular effects of toxicity should be studied and used as a basis for the selective development of future toxicity tests that can replace animal testing. To this end, the systems biology approach is to be applied, consisting of an iterative cycle of biological experiments and predictive mathematical modelling. Selecting suitable parameters for the toxicological experiments will enable researchers to validate their findings, using existing reference data, if applicable.

3. Grant Recipients

Applications may be filed by universities, non-academic research institutions and commercial undertakings headquartered in Germany. The participation of small and medium-sized enterprises (SMEs) is explicitly encouraged.. The European Commission's definition of SMEs can be found on the Internet at http://ec.europa.eu/enterprise/policies/sme/facts-figures-analysis/sme-definition/index_en.htm and at http://ec.europa.eu/enterprise/policies/sme/files/sme_definition/sme_user_guide_de.pdf.

Research institutions that receive their basic funding jointly from the German Federal Government and the federal states will only be granted project funds supplementing their basic funding for their additional expenses under certain conditions.

The inclusion and analysis of integrated omics data and their utilization in systems biology research requires special expertise with respect to both experiment and theory. For successfully implementing the e:ToP pilot projects, it is therefore desirable that grant recipients cooperate with partners that have relevant experience in the required fields, particularly in bioinformatics and systems biology. On the part of the representatives of the omics area, a concept as well as proven expertise and existing infrastructure for managing the generated data is essential.

3.1 Project Management

In collaborative projects, successfully resolving complex, multidisciplinary issues requires particularly close and efficient cooperation between all the working groups involved. In order to ensure successful cooperation, a coordination structure (project management) must be established. The coordinator will manage the individual collaborative project, will represent the project to third parties, and will ensure during cooperation meetings that information is exchanged between those involved in the project, and that work planning is streamlined. The coordinator will also ensure that the mandatory project reports are submitted to BMBF/PtJ-BIO in due time. The project management structure should be tailored as required for projects involving a large number of project partners or projects with a number of different partners who are not located close to each other.

4. Prerequisites for Funding

Funding is provided for projects that bring together toxicologists and system biologists or representatives of other comparable disciplines to find a solution to a toxicological problem using mathematical modelling.

The partners in a collaborative project must regulate their joint efforts in a cooperation agreement. Before a funding decision can be made, proof of basic agreement on specific criteria set by BMBF must be furnished. Details can be found on a BMBF information leaflet – Form 0110 – at (<http://www.kp.dlr.de/profi/easy/bmbf/pdf/0110.pdf>).

Projects undertaken by large companies can only be funded if, in the absence of aid, their projects would not be implemented or not implemented to the full extent, or if public funding accelerates development considerably, i.e. if funding provides an incentive effect under Article 8 of the General Block Exemption Regulation.

In their own interest, applicants should familiarize themselves with the EU RTD Framework Programme when planning a national project. They should check whether the envisaged project has specific European components so that funding from exclusively EU sources is possible. Moreover, it should be verified whether, in the context of the planned national project, an application for supplementary funding can be submitted to the EU. The result of such examinations should be briefly described in the application for national funding.

5. Type, Scope and Rates of Funding

Funding may take the form of non-repayable grants awarded for projects. The basis for calculating the grants for universities, research and scientific establishments and comparable institutions is the project-related expenditure eligible for funding (the eligible project-related costs in the case of Helmholtz Centres and the Fraunhofer Society [FhG]), up to 100 % of which can be funded in individual cases.

The basis for calculating the grants for commercial companies is the eligible project-related costs, of which, as a rule, up to 50 % can be financed, depending on the closeness to application of the project. According to BMBF principles, industrial companies are expected to bear a reasonable share – in principle, at least 50 % of the eligible costs incurred. As per the General Block Exemption Regulation, the percentage of funding paid to small and medium sizes enterprises (SMEs) may be higher. Please note that for commercial undertakings, the threshold values listed in Article 6(1), points (e) and (g) of the General Block Exemption Regulation and the aid intensity regulated in Articles 31, 32 and 33 of the General Block Exemption Regulation must not be exceeded.

Funding may be granted for a period of up to 24 months.

6. Other Terms and Conditions for Awarding Grants

The general auxiliary terms and conditions for funds provided by BMBF to commercial companies for research and development projects on a cost basis (NKBF98) will be an integral part of the conditions of award for grants on a cost basis.

The general auxiliary conditions for grants for the promotion of projects (ANBest-P) and the special auxiliary terms and conditions for grants from the BMBF for the promotion of projects on an expenditure basis (BNBest-BMBF98) will be an integral part of the conditions of award for grants on an expenditure basis.

7. Procedure

7.1 Commissioning a Project Management Organization and Request for Documents

BMBF has commissioned the following project management organization to implement the funding measure:

Projektträger Jülich (PtJ)
Geschäftsbereich Biologie
Forschungszentrum Jülich GmbH

52425 Jülich
Germany

Your contact person is:

Dr. Vera Schulte

Tel: +49 2461 61-3926

Email: v.schulte@fz-juelich.de

Forms for funding applications, guidelines, information sheets, instructions and auxiliary terms and conditions can be found on the Internet at <http://www.kp.dlr.de/profi/easy/bmbf/index.htm>. Copies can also be requested directly from the project management organization.

Applicants are strongly advised to use the electronic application system “easy” to prepare their project outlines and formal applications for funding (<http://www.kp.dlr.de/profi/easy/>). Project outlines and applications should be drafted with a view to facilitating evaluation against the criteria listed below. Those seeking funding are advised to contact the responsible project management organization in good time.

7.2 Two-Stage Funding Process

The funding process consists of two stages.

7.2.1 Submission of Project Outlines

In the first process stage, project outlines should be sent electronically to Project Management Jülich via the Internet portal pt(outline* (<https://www.pt-it.de/ptoutline/application/etop>), following the instructions that can be found there.

Instructions for writing project outlines can be found under “Leitfaden zur Skizzenerstellung” on Project Management Jülich’s website and in pt(outline* (available in German only). They define binding requirements for project outlines.

Since there will be an international evaluation procedure, it is recommended that project outlines be submitted to Project Management Jülich in English.

In the case of collaborative projects, project outlines should be submitted with the approval of the envisaged collaboration coordinator.

A one-page project overview will be generated from data entered in an online form. In order for the electronic version to be legally valid, after submitting the application electronically, the project overview must also be submitted to the project management organization in paper form, with the signature of the collaborative project coordinator.

Entries can be made in the pt(outline* Internet portal until 23:59 on 31 January 2013. The Internet portal will be closed upon expiration of the deadline.

The deadline for submission is not a cut-off deadline. However, it may not be possible to consider project outlines received after the specified date.

No legal claim to funding can be derived from the submission of a project outline.

7.2.2 Selection of Project Outlines: Panel of Experts

The project outlines received will be evaluated with the participation of an international panel of experts against the following criteria:

- relevance of the project outline with regard to the objectives of the announcement
- scientific originality and innovative potential of the contribution
- excellence and expertise of the applicant (“track record”) and the partners involved; relevant preliminary work by all partners
- quality and functionality of the selected research structure with regard to the planned objectives (appropriateness of the size and structure of the project, quality and feasibility of time and work planning, quality of the integration, interdisciplinarity and collaborative networking of the partners)
- structure and functionality of data management
- feasibility of validating important experimental framework conditions and functional results of data analysis within a short period of time
- feasibility of the project: appropriate budget, proof of all required expertise and resources, access to data and cell material
- appropriateness of the internal structures of the collaboration for coordination and communication and for quality management for data and materials
- assessment of the information on sustainability
- international competitiveness of the project
- possibilities for utilizing research results (if applicable, transfer plan for practical application)

7.2.3 Submission of Formal Funding Applications and Decision-Making Process

In the second stage of the process, after completion of the appraisal process, the applicants of the project outlines recommended for funding will be requested to submit a formal application for funding in coordination with the envisaged coordinator. This will form the basis for the funding decision, which will be made after a final review.

Approval, payment and accounting of the funds, as well as proof and examination of proper use and, if necessary, revocation of the award and reclaiming of the funds awarded are governed by the administrative regulations pertaining to Article 44 of the Federal Budget Code (BHO) and Articles 48 to 49a of the Administrative Procedure Act (VwVfG) unless these present funding guidelines permit an alternative procedure.

7.3 Partnering Day

A partnering day will be organized in Berlin to give potential applicants an opportunity to present their project ideas and discuss them with possible project partners. The envisaged date for the partnering day is mid-November (week 46). Attendance at this event is not mandatory for the submission of project outlines in accordance with section 7.2.1. Further information on the partnering day can be found on the project management organization's website and is also available directly from the responsible contact person. If you are interested in attending this event, please contact Project Management Jülich no later than the end of September.

7.4 Status Seminar

Twelve months into the project, a status seminar should be held in order to ensure an active exchange of information between representatives of the various research approaches. Participation in the status seminars is obligatory for project coordinators, and this must be taken into account when planning travel expenses. In addition, project coordinators may be requested to participate in thematically overarching BMBF events, such as for the promotion of young investigators.

8. Entry into Force

These present funding guidelines shall enter into force on the day after their publication in the Federal Gazette (Bundesanzeiger).

Berlin, 9 August 2012

Federal Ministry
of Education and Research
Signed

Prof. Dr. Frank Laplace

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