2019 Call for Proposals

Development and integration of new experimental models relevant for research in oncology:

Optimisation of the 3R principle

The Cancer ITMO of the French National Alliance for Life and Health Sciences (AVIESAN), in collaboration with the Institut National du Cancer (French National Cancer Institute) and Inserm, implements the research section of the cancer plan.

Online submission: https://sp2013.inserm.fr/sites/eva/appels-a-projets/Pages/default.aspx
Deadline: 25th October 2018
Contact: plancancer.modelexperimentaux@inserm.fr
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1 BACKGROUND AND OBJECTIVES OF THE CALL FOR PROPOSALS

The use of animal models has led to major advances in the understanding of human cancers, their treatment, prevention and prognosis. However, there is an increasing societal pressure on the use of animal models for research and medical purposes. Yet it remains widely accepted by scientists that preclinical models are required and that their use must be more supervised. In fact, since 2010, the regulation of animal experimentation has established three fundamental principles ("3R Rule") now enshrined in European (Directive 2010/63 / EU) and French law (Decree 2013-118); Orders of February 1st, 2013). These concepts, developed by Russell & Burch in 1959, contribute to the development of alternative methods and the rational use of animals. They consist of replacing animal models with other models as much as possible; to minimise the number of animals needed for the experiments and to "refine" (improve) as much as possible the welfare of the animals used and to minimise the constraints they suffer.

As part of the Cancer Plan, ITMO Cancer wishes to strongly support the implementation of this approach in the field of oncology. For this purpose, it launches a call for proposals whose general objective is to study the mechanisms of carcinogenesis, initiation or metastatic dissemination; to identify biomarkers for prevention and early diagnosis, or new therapies by optimising the use of the “3R” principles. To address this, it is necessary to demonstrate the relevance and validity of the experimental models used or developed, by combining at least two completely distinct models (in vivo versus in vitro, induced versus spontaneous, distinct animal species, etc.). These models should be designed and established to reduce the number of animals (based on statistical models), to refine experimental procedures and/or to replace induced animal models by alternate in vitro or spontaneous models. The multiple environmental (microbiota, diet, fasting, physical activity ...) and/or micro-environmental contingencies of the tumor should be taken into consideration in the development process. Finally, the choice of the complementary models proposed should be guided by results obtained, which best mimic the human disease, or at least which take into account the constraints observed in the latter.

2 SCOPE OF THE CALL FOR PROPOSALS

Eligibility criteria:

- Combine at least two entirely distinctive experimental models

Eligible research topics:

- Characterisation and physiopathological and genetic studies of induced or spontaneous animal models, with validation of relevance for human pathology
- The development and use of non-experimental models, such as certain domestic pets spontaneously developing the same cancers as humans
- The development of in vitro models as substitutes to animal models which allow to optimise the reproduction of tumor development in vivo (ex: 2D, 3D, iPSc, organoids ...)
- The development of new diagnostic and/or therapeutic approaches
- The development of new biomarkers at different stages of the disease
Points to be noted:

The project holders are suggested to take into account of the following information:

- Ethical guidelines on animal models

- Guidelines regarding human samples in biomedical research

- Statistical recommendations
  - https://www.nc3rs.org.uk/experimental-design
  - https://www.nc3rs.org.uk/experimental-designstatistics

Out of scope research projects:

- Clinical trial projects.

3 CRITERIA FOR ELIGIBILITY AND PROJECT EVALUATION

For each project submitted, the participating teams shall designate a scientific coordinator for the project. In addition to his or her scientific and technical role, the coordinator is responsible for setting up the process for collaboration between the participating teams, for the production of the required documents (reports and assessments), holding meetings, the progress and the communication of results. Applications from early-stage scientific coordinators are strongly encouraged.

For each project submitted, the participating teams shall designate their managing body (which can differ from the research body that the coordinator belongs to). The management body is contractually liable to Inserm for implementing the contract, forwarding all of the financial and scientific reports provided for in the agreement.

3.1 Criteria for eligibility

In order to be eligible, the projects must satisfy the following conditions:

- The project must meet the objectives of this call for proposals and fall within one of the themes identified in section 2,
- The project must have a duration of 24 to 36 months,
- The project may be undertaken by a single team or a consortium consisting of maximum 3 teams which belong to different research themes, research units, and/or bodies,
- The project Coordinator must be a permanent researcher of a public organisation or an institution of higher education or a public health institute or a recognised public utility research foundation. He/she must spend at least 30% of his/her time on the project,
- The Coordinator's managing body should be a public research institute, an institution of higher education or a public health institution or a recognised public utility research foundation. The managing body of the project Coordinator must not be a charity. For clarification, you can refer to section 5.3,
- The application form must be duly completed and include all the required documents according to the submission procedures mentioned in section 6.
Each team can submit only one application (regardless of their status as a project co-ordinator or a member of the consortium).

3.2 Criteria for evaluation

After the eligibility criteria have been verified, the applications are subject to a written evaluation by international experts and by at least one reviewer from the evaluation committee, the members of which do not take part in any project. Projects which do not meet the eligibility criteria will not be assessed. After publication of the list of selected projects, the list of members of the evaluation committee will be posted on the EVA website of Inserm. The opinions of the committee and experts will be sent at the request of the project scientific coordinator.

The criteria for evaluation are:

- **Innovation and development:**
  - Innovative nature (strategy, concept, technology, etc.),
  - Perspectives in terms of future developments.

- **Scientific qualities:**
  - Project relevance and originality,
  - Positioning of the project in the national and international context,
  - Clarity of the objectives.

- **Coordinator and participating teams:**
  - Skills of the coordinator in his/her discipline
  - Complementarity and/or multi-disciplinarity of the various teams associated with the project,
  - Organisation of collaboration between candidate groups, planning review document production, holding follow up meetings and formatting results.

- **Methodology and feasibility:**
  - Methodological relevance,
  - Project environment (human resources, host structure),
  - Credibility of the project’s schedule and of the financing requested.
4 CALENDAR OF THE CALL FOR PROPOSALS

| Date of publication of the call for proposals | July 2018 |
| Opening of project submission website | September 25th, 2018 |
| Deadline for submitting application files (ONLY ELECTRONIC FILES ARE ACCEPTED) | October 25th, 2018 |
| Tentative meeting date for the evaluation committee | February 2019 |
| Tentative date for publishing the results¹ | March 2019 |

5 ADMINISTRATIVE AND FINANCIAL RULES

Preliminary article - Definitions:

Funding allocation instrument (Grant Agreement): Funding agreement or letter by which Inserm notifies the Managing Body of its rights and obligations with respect to the implementation/progress of the selected project. The Grant Agreement is in the form of a notification letter if the body managing the grant is Inserm. These two documents are hereafter referred to with the generic term "Grant Agreement".

Research Association: A private non-profit organisation devoting at least 50% of its main activity to research.

Managing Body: Research body managing the grant to conduct the research project as submitted in the Application File. The Managing Body is contractually responsible for implementing the contract and compiling all the scientific and financial reports stipulated in the Grant Agreement.

Project Coordinator: The person responsible for the scientific conduct of the Project as designated in the Grant Agreement.

Research body: This term refers to all entities such as public research institutions (EPST, EPIC, etc.), institutions of higher learning (universities, etc.), research foundations, healthcare establishments, and any other body involved in research.

Partner: A research team contributing to the Research Project.

Project: Research project provided in the scientist's Application File and selected by Inserm for funding within the framework of the Cancer Plan.

Regulation: These financial rules with their appendices.

5.1 Scope

These Rules apply to Managing Bodies that are allocated a grant by Inserm to conduct a Research Project, selected in a tender for projects launched by Inserm. Inserm sets down the tender procedures under the aegis of the following divisions: ITMO Cancer and the Département de l’Évaluation et du Suivi des Programmes (DESP, Department of Programme Evaluation and Monitoring) within the framework of the Cancer Plan 2014-2019.

¹ Results will be published on the EVA website : https://www.eva3.inserm.fr
5.2 Contents

Inserm grants the funding once the Project is selected based on the Application File submitted by the Coordinator according to the criteria for eligibility and evaluation of the text of the corresponding tender for projects.

The Application File must include:
- A scientific file,
- The Project’s budget broken down in the financial appendices. The financial annexe should be uploaded as an Excel document AND as a signed and stamped PDF version,
- The CVs of the Project Coordinator and the Director(s) of any associated team(s) (all in a single file),
- The Administrative Form to be filled out online on the dedicated Application File Submission website,
- The bank statement of each Managing body.

For research charities, the following complementary documents should be appended to the Application File:
- Previous year’s accounts together with forecasts and a financial plan, all following Inserm models.

Incomplete application files will be deemed ineligible

5.3 Managing Bodies

Teams belong to the following bodies:
- Public-sector research institutions (EPST, EPIC, etc.),
- Institutions of higher learning (universities, etc.),
- Public-sector healthcare establishments,
- Research foundations recognised of public utility,
- International research organisations whose teams work on the French territory.

Public research teams affiliated with a public-sector research institution, institution of higher learning or a public-sector healthcare establishment must have their grant managed by their associated public body or one of the mixed administrators of their structure.

The participation of industrial partners and/or foreign teams is possible as long as they provide their own funding in the Project.

The funding of charities (as defined under the 1901 Law) not classified as Research Charities is not allowed. Management via a charity is only possible if it justifies research activity and has specific means dedicated to this research activity. Similarly, Inserm will check the capacity of charities to finance the counterpart of the work remaining at their expense. During the selection process, Inserm may check that any charity partners in the Research Project are able to finance the part of the research cost not covered by the Inserm grant. When administrative and financial files are being finalised, charities allocated a grant may be asked for further information.
5.4 **Coordinator**

If there are multiple teams involved\(^2\), a Project Coordinator must be appointed. Each partner team appoints a scientific leader.

In addition to his/her scientific and technical role, the Coordinator is responsible for organising the collaboration between participating teams and meetings as well as monitoring progress and communicating results. He/she is responsible for compiling the required reports and sending them to Inserm.

The Coordinator must:

- Be a **statutory employee** of a public-sector research body, a public institution of higher learning or a public healthcare institution and
- Devote **at least 30%** of his/her time to the Project.

5.5 **Duration of the Project**

The Managing Body and the Coordinator commit to the Project being completed within the time frame stipulated in the Granting Act not withstanding possible changes in duration detailed in Article 6.

This duration corresponds to that in which **expenses must be assumed and paid**.

⚠️ The Project must begin before 30th June 2019.

5.6 **Granting Act**

5.6.1 **Form of the Act**

The Act takes the form of:

- Either a grant agreement signed by the Managing Body and Inserm,
- Or a notification letter sent to the beneficiaries if the Managing Body is Inserm.

If the project involves several teams belonging to different management bodies, and benefiting from a part of the allocated funds, each managing body will sign an agreement concluded with Inserm.

5.6.2 **Compulsory Information that must be mentioned in the Granting Act**

The Granting Act is compiled by Inserm on the basis of information in the Application File and the text of the corresponding Tender for Projects.

It must include the following information:

- **Title of the Project in French and in English**,  
- **Duration of the Project**,  
- **Duration of the Granting Act**,  
- **Partners involved in the Project and the Coordinator**,  

\(^2\) Refer to eligibility criteria
The total sum granted and how it is to be paid,
The obligation to send Inserm the reports mentioned in Article Sh of the Rules. How and when these are to be sent are stipulated in the Granting Act,

Appendices to the Granting Act:
- Appendix 1: summary of the Project as stipulated in the Application File,
- Appendix 2: budget of the Project,
- Appendix 3: model of the financial justification.

5.6.3 Documents constituting the Granting Act
The documents that make up the Granting Act have the following order of precedence, especially in the event of conflicting provisions:

- The Granting Act and its appendices,
- The Rules.

5.6.4 Special provisions
Inserm and the Managing Body may include in the Granting Act special obligations and/or exemptions from the Rules that are justified either:

- by specificities of the funded Project, or
- by modification of the Project in the framework of the Tender for Projects, or
- by an agreement between Inserm and one or more of its partners.

5.6.5 Notification of the Granting Act
The Granting Act is notified by a letter from Inserm.

5.6.6 Modification of the Granting Act
Inserm will compile and sign an additional clause for any modification of the provisions of the Granting Act. However, prolongation of the duration of the Project, agreed to on an exceptional basis, is notified by a simple letter sent to the grant's Coordinator or Managing Body. The request for extension must be sent in writing by the Coordinator within 6 months of the end of the Granting Act.

The extension cannot exceed 12 months.

5.7 Grant allocated

5.7.1 Calculation of the amount of the funding
When the total sum granted is identical to that asked for in the Application File, it includes the budgetary appendix compiled by the Coordinator when the application is submitted.

If the total sum granted by Inserm differs from that asked for in the Application File, Inserm sends the Coordinator an E-mail with the total amount of the grant that it is intending to attribute to conduct the Project. In this case, a new financial appendix is compiled, dated and signed by the Managing Body. Then the Coordinator must conduct the Research Project in line with the instructions of Inserm.

In the event of refusal to compile a new financial appendix or failure to answer within one month of Inserm sending the E-mail, no grant will be attributed.

The grant attributed cannot be less than 25,000 € per team participating in the Project for its entire duration. No maximum amount is set. Only the evaluation criteria and the consistency of the proposal
will be considered. For charities, a first payment is made when the Agreement is signed. Subsequent payments, up to a limit of 80% of the grant, are made after validation of the interim reports (scientific and financial).

5.7.2 Value Added Tax
Because of the absence of counterpart to Inserm's financial support and applying the provisions of fiscal instruction 3A-4-08 of 13 June 2008 from the Public Finances Directorate, the grant attributed by Inserm is not subject to VAT.

5.7.3 Payment

5.7.3.1 Schedule
For Managing Bodies other than Inserm, the total sum is allocated at the starting date of the Project and upon signing the Agreement.
When the Managing Body is Inserm, the credits corresponding to the funding are allocated in annual installments.

5.7.3.2 Suspension of payment
If a project is yet to start on the date of the first scientific report is produced, Inserm shall notify the Managing Body of its shortcomings by sending a registered letter with acknowledgement of receipt. This letter shall direct the Managing Body to remedy the difficulties noted within the two (2) calendar months following the receipt of the letter.

After this period has elapsed, if the project has still not started, termination is declared according to the procedures described in the funding allocation instrument.

5.7.4 Use of the grant
The managing body must use the grant allocated by INSERM strictly for the project identified in the Grant Agreement.

At the end of the research project, the amount not paid/mandated, shall be reimbursed to Inserm within a maximum period of ninety (90) calendar days.

5.7.5 Eligible expenditure

The expenses must be directly related to the Project, strictly necessary for its implementation and duly substantiated.

5.7.5.1 Capital expenditure

*Expenditure on scientific equipment, excluding spending on office automation and furniture, is eligible.*
In the particular context of this Call for Proposals, Inserm only finances capital expenditure up to a maximum of €50,000 excl. VAT per team. For any expenditure of a higher amount, co-financing should be considered.
5.7.5.2  **Staff expenditure**
Expenditure for non-permanent staff is eligible.

For private-law managing bodies, expenditure for staff on permanent contracts is eligible when they are assigned to the Project for 100% of their working time within the strict framework of its implementation. It must be possible to prove this assignment to the project.

The **funding of PhD contracts is not permitted. Expenditure on staff allocated to administrative functions is not eligible.**

5.7.5.3  **Operating expenditure**

a.  **Services and outsourcing**

The Coordinator may use third-party service providers or subcontractors to perform part of the work financed by Inserm. However, the said services or subcontracting must be necessary for the project and not exceed 50% of the amount of the funding granted. The work performed by third parties is the responsibility of the Managing Body.

b.  **Consortium agreement drafting costs**

The costs of drafting the consortium agreement are eligible if the conditions of the article 5.13 (Intellectual Property - Consortium Agreement) hereafter in these Regulations are met.

c.  **Other operating expenditure**

The following other operating expenditure is eligible:

- Cost of consumables;
- Expenses incurred for travel by researchers (assignments) within the framework and for the purposes of carrying out the Research Project;
- The intellectual property costs of patents or licences resulting from implementation of the Project;
- Expenditure justified by an internal billing procedure.

5.7.5.4  **Management fees**

Part of the administrative costs of the Managing Body generated by the Project may be included in the funded expenditure. This part of the general administration fee is **capped at 8% of the project grant as regards the total cost of eligible expenditure** of the Managing Body and it does not require financial proof.

5.7.5.5  **VAT expenditure**

For managing bodies subject to or partially subject to VAT, the non-recoverable VAT portion of the project constitutes eligible expenditure, on presentation of proof of the non-recoverable VAT rate.
5.7.6 Fungibility

The grant paid by Inserm is fungible within the operating expenditure item. The budget can only be transferred to staff costs after exceptional agreement by Inserm.

5.7.7 Other provisions

If the amount of the grant paid by Inserm does not cover all of the expenses related to conduct of the Project, the Managing Body undertakes to supplement the funding, allowing its proper implementation, either from its own resources or through one or more co-financing arrangements.

In the latter case, the Managing Body will inform Inserm, in the event of co-financing obtained after notification of the agreement, of the name of the co-financer and the amount allocated to the project.

5.8 Scientific and financial reports

Reports must be written in French without fail.

5.8.1 Scientific reports

The Coordinator shall forward the scientific reports according to the procedures defined in the funding allocation instrument.

Their transmission shall occur in keeping with the following schedule:

- A progress report six (6) months after the start;
- A mid-term project report for proposals exceeding two (2) years;
- A final report no later than four (4) months after the end of the project.

Failure to produce interim or final scientific reports shall give rise to reimbursement of all the sums paid by Inserm.

The scientific evaluation of the interim and final reports may lead Inserm to request additional information, to suspend or terminate the financial support granted in the event of non-compliance with the Project or the use of funding for another project.

5.8.2 Financial reports

Financial reports are prepared in accordance with the procedures set out in the funding allocation instrument and the Regulations; they present expenditures made/mandated during the duration of the Project.

Charities shall send a mid-term financial report of the funding allocation instrument.

The managing bodies shall submit a final financial report no later than four (4) months after the end of the agreement.

The financial reports are signed by the person authorised to certify the expenses within the Managing Body.

They are sent to Inserm at the same time as the scientific report by each Managing Body of the grant.
Expenditure related to the certification of expenditure by an auditor who is external to the Managing Body is eligible expenditure.

At the end of the project, in the event of a balance remaining on the sum paid by Inserm, the Managing Body will transfer the balance to Inserm.

5.9 **Other undertakings by the Coordinator and each Managing Body**

The Coordinator is required to inform Inserm of any substantial modification to the Research Project compared with the content of the application file, or the funding allocation instrument, or difficulties impeding conduct of the Research Project.

The Coordinator also undertakes to participate actively in project monitoring operations organised by Inserm/Cancer ITMO (symposia feedback seminars, etc.)

The Managing Body shall inform Inserm in the event of a change of address or bank details.

5.10 **Authorising Officer - Designated Public Accountant**

The Authorising Officer for grants and credit transfers is the Chief Executive Officer of Inserm and, by delegation, the Director of the Department of Financial Affairs.

The Designated Public Accountant for payments is the Chief Accountant of Inserm.

5.11 **Technical and financial control**

During the term of the agreement, Inserm reserves the right to organise a site visit in consultation with the Managing Body and the Project Coordinator.

The use of the grant under the funding allocation instrument may be subject, during the life of the Project and for two (2) years after its expiry, to a control or an audit by Inserm, carried out by Inserm or by a firm mandated by it for this purpose, in respect of documents and/or on site.

The Managing Body must be able to demonstrate the allocation to the project of the funded staff as well as all the expenditure made using the grant.

The Managing Body must be able to provide all administrative, accounting supporting and legal documents relating to use of the grant.

It should be noted that, as these are public funds, this funding may be subject to control by the various state supervisory bodies.
5.12 Publications - Communication

5.12.1 Publications

All the publications resulting from the research project shall mention the financial support in the following terms:

"With the financial support of the Cancer ITMO of the French Alliance for Life Sciences and Health (AVIESAN) under the Cancer Plan. »

These publications are sent to Inserm for information as soon as possible and no later than five (5) days after publication.

5.12.2 Dissemination of a summary of the project

The Coordinator authorises the dissemination of abstracts in English and French for the project contained in the application file. The text will be sent by e-mail to the Coordinator, before any dissemination, for validation of its content. If there is no answer within forty-five (45) days of this transmission, validation will be deemed to have been obtained.

5.12.3 Production of an impact analysis

The Coordinator undertakes to produce, for subsequent dissemination on the Cancer ITMO website, an impact study summarising the contribution to the fight against cancer made by the funded project.

5.13 Intellectual property - consortium agreement

Inserm does not acquire any intellectual property rights as a financer of calls for proposals and grants. These intellectual property rights concerning the works and the results stemming from the Project are acquired by the project’s managing bodies. In the event of multiple managing bodies, the latter agree on the distribution of intellectual property rights.

The drafting of a consortium agreement is strongly recommended when:

- The total amount of the grant is more than €250,000;
- More than three partners are involved in the project.

It becomes mandatory as soon as a private-law Managing Body becomes a partner in the Project.

5.14 Confidentiality

Inserm undertakes to keep confidential the information obtained during the conduct of the Project, in particular, those contained in the activity report, hereinafter referred to as the "information". In particular, Inserm undertakes to refrain from divulging any item to any third party, and in any form whatsoever without the written agreement of the Coordinator, except during the Steering Committee of the Cancer Plan.

However, Inserm will no longer be bound to secrecy for a particular item of information when it can prove that:
The information is available in the public domain without any breach of the funding allocation instrument or the Regulations;
The information is already known to Inserm on the date of signing of the agreement;
The information becomes freely available from another source which has the right to freely dispose of it.

5.15 Protection of personal data

The personal information collected in the application file shall be computerised to enable processing of the files and the administrative and financial follow-up of the Research Projects. In accordance with the law "Informatique et Libertés" of 6 January 1978 amended in 2004 (French data protection act), people whose data are collected have a right of access, rectification and deletion of information concerning them. They may exercise the said rights by contacting Inserm, Département des affaires juridiques, 101 rue de Tolbiac 75013 PARIS

5.16 Settlement of disputes

Should a dispute arise between Inserm and the Managing Body concerning the interpretation or performance of the funding allocation instrument, they undertake to submit their dispute, prior to any court proceedings, to conciliators appointed by each of them, unless they agree on the appointment of a single conciliator.

The conciliator(s) will endeavour to resolve the difficulties and to have the party accept an amicable solution within a period of sixty (60) days from the date of appointment of the conciliator(s).

In the absence of conciliation, the dispute related to application of the funding allocation instrument shall be referred to the administrative judge.

5.17 Implementation of the Regulations

These Regulations shall come into effect on the date of their publication and shall apply to grants awarded by Inserm within the framework of the scheduling of the 2019 Call for Proposals concerning "Experimental models".

6 PROCEDURES FOR SUBMISSION

Submitting your application file consists only in:

Registration on the EVA3 website of Inserm and submission of the application file online.

6.1 Application file

The application file must include all the items required and necessary for the scientific, technical and financial evaluation of the project. It is recommended to produce a scientific and technical description of the project proposal in English as the evaluation is conducted by non-French speakers. In the event that the scientific and technical description is written in French, an English translation may be requested within a time frame compatible with the deadlines of the evaluation process.

The application file comprises 5 documents:
The completed scientific document (to be downloaded from the EVA website),
The financial appendices completed (download the file in Excel and PDF format from the EVA website, the PDF version uploaded must be signed AND stamped),
The CVs of the Coordinator and the Associated Team Leader(s) to be included in a single document (in PDF format),
The administrative form completed online on the EVA website,
The Bank Identification Statement of each Managing Body

⚠️ Incomplete application files will be deemed ineligible.

6.2 Electronic submission procedure

Website: https://www.eva3.inserm.fr

This submission procedure, from the Inserm EVA website, includes:

- Identification of the applicant (surname, first name and email) allowing the receipt of a user code and password giving access to a secure personal space on EVA,
- The administrative form to be completed online,
- The uploading of the requested documents (scientific document in PDF format, financial appendices in Excel format, financial appendices in PDF format which must be stamped and signed by the legal representative, and CV of the Project Coordinator and managers of the participating teams).

Submission deadline: 25th October 2018

You are strongly advised not to wait until the deadline for closure of the Call for Proposals to submit your project proposal.

⚠️ Incomplete application files will be deemed ineligible.

6.3 Paper format

No application file in paper format.

7 PUBLICATION OF THE RESULTS

The list of projects funded will be published on the EVA website of INSERM. For these projects, the abstract (in French) will be published at a later stage, and each applicant will be contacted in order to confirm the content or provide a publishable version. Results will be communicated in writing to the Coordinators.
8 CONTACTS

For further information, please contact:

- for scientific and technical aspects: plancancer.modelexperimentaux@inserm.fr
- for administrative and financial aspects: plancancer.daf@inserm.fr
- for problems relating to the electronic submission: eva@inserm.fr

An applicant guide is available on the EVA website, please feel free to consult it.