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# "Programme et Équipement Prioritaire de Recherche"

## Women's Health, Couples' Health

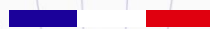
### "Call for applications to form research consortia on Infertility and Endometriosis"

The call for applications is open until April 30, 2024 at 5:00 pm (Paris time).

Address for consultation: [https://eva3-accueil.inserm.fr/sites/eva/appels-a-projets/Pages/pepr-sante\\_femmes\\_et\\_couples.aspx](https://eva3-accueil.inserm.fr/sites/eva/appels-a-projets/Pages/pepr-sante_femmes_et_couples.aspx)

**CALL FOR APPLICATIONS**

January 30, 2024



## Summary

The government has entrusted Inserm with the task of managing a "Women's Health, Couples' Health" PEPR, designed to enable the implementation of the relevant research initiatives set out in the National Strategy to Combat Endometriosis and in the Report on the Causes of Infertility - Towards a National Strategy to Combat Infertility. This PEPR will support research into the fundamental mechanisms at play, as well as clinical, epidemiological and human and social science research, and pave the way for key innovations in this field. It should contribute to the structuring of French research in this field.

The Women's Health, Couples' Health program is divided into research themes developed within open research projects (in response to calls for applications) and a targeted project. The present call for applications for Women's Health, Couples' Health concerns open projects.

In France today, as in most developed countries, one couple in four who wishes to have children is unable to achieve pregnancy after 12 months of trying, making infertility a major public health issue. Infertility, whether male or female, is very often linked to medical causes or environmental factors.

Endometriosis is a chronic hormone-dependent gynecological disease affecting women of childbearing age. It is a major cause of infertility. However, female infertility is only one of the many consequences of endometriosis, which causes pain that is often incapacitating and prevents women from carrying out their daily activities. In France, it is estimated that around 2 million women of childbearing age suffer from endometriosis, i.e. one woman in 10.

Projects submitted in response to this Call for Applications (CCA) must address one or more of the challenges listed in the document. The aim is for the selected teams to become part of an Infertility consortium or an Endometriosis consortium.

**This call is open to all French teams, whatever their field of research, with a potential interest in the themes described below, including teams not previously specializing in these areas.**

The Call for Applications will consist of two phases:

- a first phase for submitting letters of intent. The analysis of the applications will be entrusted to an independent international jury corresponding to the members of the Scientific Advisory Board (SAB) of PEPR Women's Health, Couples' Health. At the end of this pre-selection phase, the SAB will propose the list of teams who will participate in the Infertility consortium or the Endometriosis consortium.

- In a second phase, each consortium will draw up a work program under the supervision of the SAB. The finalized project will be evaluated by an independent international jury appointed by ANR.

This AAC is designed to support large-scale projects lasting 4 to 5 years.

## Keywords

Infertility, endometriosis, adenomyosis, gametes, assisted reproduction, epidemiology, human and social sciences, environment, exposure, biomarkers.

# Important dates

## Closing of call for consortium applications

The elements of the submission file must be submitted in electronic form by:

**April 30, 2024 at 5pm (Paris time)**

on the website: [https://eva3-accueil.inserm.fr/sites/eva/appels-a-projets/Pages/pepr-sante\\_femmes\\_et\\_couples.aspx](https://eva3-accueil.inserm.fr/sites/eva/appels-a-projets/Pages/pepr-sante_femmes_et_couples.aspx)

It is necessary to read carefully the whole of this document and the instructions available on the submission site:  
[https://eva3-accueil.inserm.fr/sites/eva/appels-a-projets/Pages/pepr-sante\\_femmes\\_et\\_couples.aspx](https://eva3-accueil.inserm.fr/sites/eva/appels-a-projets/Pages/pepr-sante_femmes_et_couples.aspx)

## Contacts

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# 1. Background and objectives of the call for applications

## 1.1. Context

The government has entrusted Inserm with the task of managing a "Women's Health, Couples' Health" Program (PEPR), designed to enable the implementation of the relevant research initiatives set out in the National Strategy to Combat Endometriosis and in the Report on the Causes of Infertility - Towards a National Strategy to Combat Infertility. This PEPR will support research into the fundamental mechanisms at play, as well as clinical, epidemiological and human and social science research, and pave the way for key innovations in this field. It should contribute to the structuring of French research in this field.

The Women's Health, Couples' Health program is divided into research themes developed within open research projects (in response to a call for applications) and a targeted project. The present " Women's Health, Couples' Health " Call for Applications concerns open projects.

It is very important to mention from the outset that this AAC is open **to any French team** potentially interested in the themes described below, **whatever their institutional affiliation and field of research, including teams hitherto unspecialized in these fields.**

## 1.2. Objectives of the call for applications

Today in France, as in most developed countries, one couple in four who wishes to have children is unable to achieve pregnancy after 12 months of trying.

With 3.3 million people directly concerned in France, infertility is a major public health issue. In France, as in all industrialized countries, the increase in infertility is first and foremost the result of the rise in the reproductive age. In four decades, this age has increased by five years. In 2019, French women had their first child at an average age of 29. As fertility gradually declines from the age of 30, so-called "late" pregnancies mechanically increase the risk of infertility.

This increase in the age of childbearing is the result of a number of societal factors, such as the generalization of women's work, the use of contraceptive techniques, the increase in the age of access to stable employment for both men and women, and the ignorance of many couples about the decline in fertility with age, combined with excessive confidence in the performance of medically assisted reproduction techniques. All these factors have led to an increased demand for medical support at an increasingly late stage, limiting the success rate.

Infertility is very often linked to medical causes. Endometriosis is one of the main causes of infertility in France. Polycystic ovary syndrome is the most frequent cause of menstrual cycle disorders and absence of ovulation. Infertility in men can be endocrine, testicular or linked to lesions of the genital tract. It is suspected that many of these causes have a genetic basis, which is often under-diagnosed.

At more distant levels, infertility and its medical causes may be due to environmental factors, such as endocrine disruptors, a stressful lifestyle or disrupted biological rhythms such as shift work. In addition, nutritional factors such as extreme body mass, or drug use, have a negative impact on fertility in both men and women.

Endometriosis is a chronic, hormone-dependent gynecological disease of women of childbearing age. It is characterized by the presence of endometrial-like tissue outside the uterine cavity. Endometriosis lesions, located outside the uterine cavity, react to hormonal variations in the menstrual cycle. This causes bleeding, nodules or cysts in the areas where they are located, as well as inflammatory reactions with the potential formation of scar tissue and adhesions between neighboring organs. Endometriosis is a heterogeneous disease with three widely recognized phenotypes: superficial endometriosis, ovarian endometrioma and deep endometriosis. The causes and pathophysiology of endometriosis are still poorly understood. Endometriosis affects some 190 million women worldwide. In France, it is estimated that around 2 million women of childbearing age suffer from endometriosis, i.e., one in 10. Endometriosis causes pain that is often incapacitating and prevents women from carrying out their daily activities. In addition to the cost of medical treatment, its social and economic impact is considerable and largely underestimated.

Adenomyosis is also a hormone-dependent uterine disease characterized by the presence of endometrial-like tissue within the myometrium, generally causing pain, abnormal uterine bleeding and infertility. Its prevalence is estimated at around 20% in women of childbearing age.

The call for applications is structured around these two major themes:

- Axis 1: Infertility.
- Axis 2: Endometriosis.

The aim of this call is to form two consortia, one on infertility, the other on endometriosis. The respective size of these two consortia is not fixed in advance, and may depend on the quality of the applications received for each axis.

## 1.3. Procedure of the call for applications

The Executive Committee of the PEPR Women's Health, Couples' Health, made up of the Program Directors (i.e., the Program Scientific Manager and the directors of the "Cell Biology, Development, Evolution" and "Public Health" Thematic Institutes) and the pilots of the axes, has prepared the text of this Call for Applications.

During the first phase of this call for applications, the letters of intent will be analyzed by an international jury made up of members of the International Scientific Advisory Board (SAB) of the PEPR Women's Health, Couples' Health. The jury will evaluate the scientific quality of the proposals, and assess whether the projects are in line with the PEPR objectives, and whether they can be integrated into a multidisciplinary consortium.

The jury will draw up a list of projects, leading to the proposal of two consortia on Infertility and Endometriosis, respectively.

Within each consortium, the selected teams will then be invited to draw up a joint work program under the responsibility of a coordinator.

The final program will be submitted to ANR for evaluation by an independent international jury.

The operational team will propose to the General Secretariat for Investment the composition of the two consortia to be financed, and the amount of aid that could be allocated to them.

# 2. Call themes and expected projects

## 2.1. Themes

Letters of intent should address one or more of the challenges described below.

**Challenges are grouped into 2 categories:**

- Axis 1: Infertility.
- Axis 2: Endometriosis.

### Axis 1: Infertility

In this context, the Women's Health, Couples' Health program is looking for projects that respond to one or other of the following challenges. **The examples given within each group of challenges are not limitative.**

#### *Challenges group INF1 - Epidemiology and environmental factors*

- *Examples:*
  - *Measuring infertility in the general population.*
  - *Identify the effects, mode(s) of action and underlying molecular mechanisms of environmental factors, potentially including plant protection products such as chlordecone, affecting fertility.*
  - *Carry out mechanistic studies to better understand the role of lifestyle factors in infertility.*

#### *Challenges group INF2 - Preserving and restoring fertility*

- *Examples:*
  - *Minimizing the impact of drugs on germ cells.*
  - *Improve fertility preservation methods.*
  - *Restore fertility through medication or transplantation.*

#### *Challenges group INF3 - Assisted reproductive technologies*

- *Examples:*
  - *Improve gamete quality.*

- *Improve embryo quality.*
- *Better understanding of the implantation window.*

#### *Challenges group INF4 – Physiopathology, Molecular and Cellular Mechanisms of Infertility*

- *Examples:*
  - *Identify the mechanisms of diseases such as polycystic ovary syndrome, ovarian failure and severe male infertility.*
  - *Better understand the regulation of spermatogenesis, and the role of male aging in gamete quality.*
  - *Better understand the molecular and cellular mechanisms of oocyte formation, fertilization and blastocyst formation, using innovative approaches.*
  - *Understand the origin of cellular defects often observed during preimplantation development.*
  - *Better understand the mechanisms of hypothalamic-pituitary control of the reproductive axis.*

#### *Challenges group INF5 - Human and social sciences*

- *Examples:*
  - *Study emerging societal demands and practices that can promote the well-being of people suffering from infertility.*
  - *Study social inequalities in the management of infertility.*
  - *Study the economic consequences of infertility.*

## **Axis 2: Endometriosis**

In this context, the Women's Health, Couples' Health program is looking for projects that respond to one or other of the following challenges. **The examples given within each group of challenges are not limitative.**

Preamble:

- The inclusion of **adenomyosis** in research projects is recommended whenever possible.
- The study of the **heterogeneous nature** of endometriosis is strongly encouraged: pathological, clinical, cellular and molecular.
- Finally, the study of the characteristics of endometriosis at **different stages of life** is also encouraged.

#### *Challenges group ENDO1 – Clinical Research*

- *Examples:*
  - *Optimize early diagnosis of the disease.*
  - *Develop, optimize and standardize therapeutic strategies.*
  - *Study the consequences of endometriosis on quality of life and the risk of long-term chronic pathologies.*
  - *Develop knowledge of the evolution, progression and natural history of the disease.*

#### *Challenges group ENDO2 – Physiopathology, Molecular and Cellular Mechanisms of Endometriosis*

- *Examples:*
  - *Optimize and/or develop innovative in vitro/in vivo/ex vivo models that are more representative of disease and lesions.*
  - *Develop knowledge of the mechanisms of pathogenesis and the physiology of the disease, for example in the following areas: Cellular, molecular and hormonal mechanisms; Genetics, epigenetics; Inflammation, immunity, microbiota; Environmental factors; Mechanisms of pain; Mechanisms of infertility.*

#### *Challenges group ENDO3 - Human and social sciences*

- *Examples:*



- *Study emerging societal demands and practices that can promote the well-being of endometriosis sufferers.*
- *Study social inequalities in the management of endometriosis.*
- *Study the economic consequences of endometriosis.*

## 2.2. Main features of the proposals

This call for applications for the Women's Health, Couples' Health program is addressed to the entire scientific community interested in infertility and/or endometriosis. **As mentioned above, teams not previously specializing in these fields are also encouraged to submit a letter of intent if they are in a position to propose significant contributions in the areas covered by the PEPR. This call is open to French teams only, regardless of their institutional affiliation.**

Letters of intent may be submitted by a **single team**, or by a **group of 2 or 3 teams maximum**. By team we mean a project-team, which must be made up of members of the same research unit. In the case of a letter of intent submitted by a group of teams, the proposed projects must target at least two challenges belonging to different groups (e.g., groups INF1 and INF3, or ENDO1 and ENDO3). **Note also that the jury is free to select only some of the teams in this group.**

**The aim is for the selected teams to join an Infertility consortium or an Endometriosis consortium. These interdisciplinary consortia will then each draw up a joint work program.**

Projects must fall within either the Infertility theme or the Endometriosis theme. Each project must indicate which theme it wishes to pursue. However, the jury is free to decide on the composition of the consortia.

Projects must be programmed for a period of 4 to 5 years.

**Please note that a researcher may submit only one letter of intent in his or her name under this call for applications.**

## 3. Review of proposed projects

The main stages of the call procedure are as follows:

- Submission of letters of intent on the dedicated website;
- Examination of the admissibility of applications according to the criteria set out in § 3.1;
- Applications submitted for this AAC must briefly describe:
  - The proposed scientific project (context, call, methodology, expected impact);
  - The context, scientific objectives and main thrusts of the team's current research topics;
  - How the project fits in with the call;
  - Tools and human resources available for the project;
  - Partners (existing or to be identified) needed to carry out the project;

and contain:

- The 10 best publications of the teams involved over the last five years;
- Short curricula vitae of the principal investigator (or principal investigators if the letter of intent is submitted by a group of teams).
- The analysis of the letters of intent will be entrusted to an independent international jury corresponding to the members of the SAB of the PEPR Women's Health, Couples' Health.

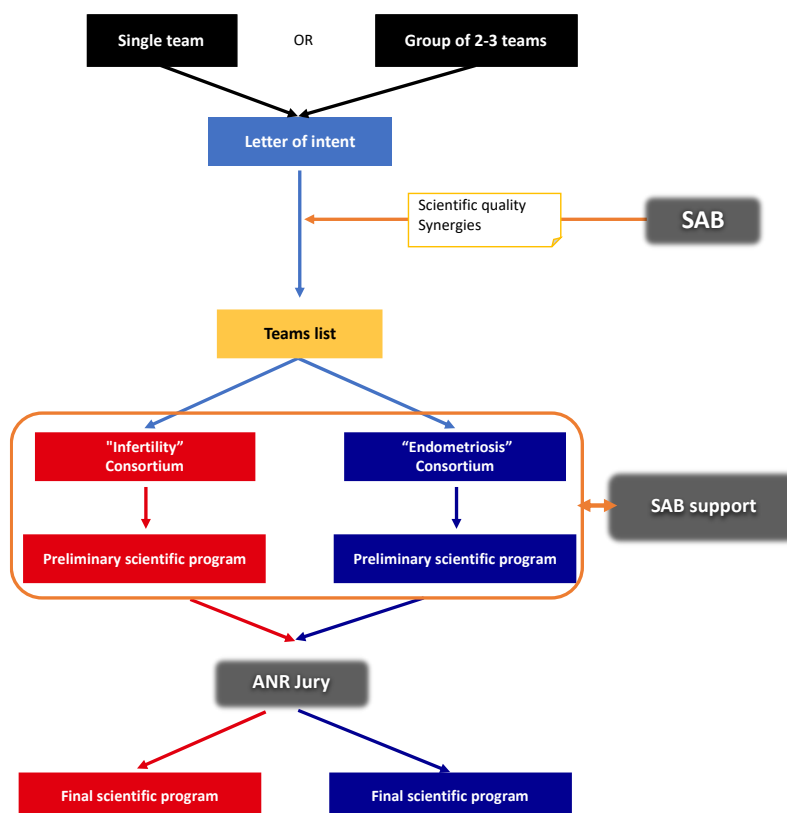
At the end of this pre-selection phase, the SAB will propose the list of teams that will participate in the consortium.

**It is important to bear in mind that in the case of proposals submitted by a group of teams, the jury will be free to select only some of the teams.**

In a second phase, the consortia will jointly draw up a work program under the supervision of the SAB. The finalized program will be evaluated by an independent international jury appointed by the ANR. The program will start after final validation by the General Secretariat for Investment.

The diagram below summarizes the entire procedure.





### 3.1. Eligibility criteria

The file must be submitted in full on the submission site before the call closing date and time.

The submission file for the call must be in unprotected PDF format and must not exceed 5 pages (excluding the cover page and the CV(s)), minimum font size: 11, Arial. Any document exceeding 5 pages will automatically render the application inadmissible.

### 3.2. Analysis criteria

The proposed project must fall within the scope of the call described in § 1.2;

The project must address one or more of the themes defined in § 2.1;

### 3.3. Evaluation criteria for letters of intent in response to the call

#### 1) Excellence and scientific ambition of the project described in the letter of intent

- Clarity of research objectives and hypotheses;
- Innovative character, ambition, originality, methodological or conceptual break with the state of the art ;
- Relevance of methodology.

#### 2) Suitability for AAC themes.

#### 3) Quality of project leader(s)

- Competence, expertise and involvement of the project leader.

#### 4) Potential synergies within a consortium

- Relevance of the research project to the consortium project;
- Suitability of tools and human resources for the consortium project.

### 3.4. Criteria for evaluating consortia programs for funding

These criteria concern the final evaluation of consortia programs by the ANR during the second stage, but they are given here as a guideline for applicants when drafting their letter of intent in response to the call.

### **1. Excellence and scientific ambition:**

- Clarity of research objectives and hypotheses;
- Innovative character, ambition, originality, methodological or conceptual break with the state of the art;
- Relevance of methodology.

### **2. Consortium quality, resources and governance:**

- Competence, expertise and involvement of the consortium coordinator: ability to coordinate ambitious multidisciplinary consortia, academic background, international recognition;
- Quality and complementarity of the scientific consortium with regard to the project's objectives;
- Scientific, financial and human resources synergies;
- Adequacy of human and financial resources (including those requested as part of the project) in relation to objectives;
- Relevance of timetable (particularly in the case of long projects), management of scientific risks and alternative solutions, credibility of proposed milestones;
- Relevance and effectiveness of program governance (steering, organization, coordination, establishment of advisory committees, etc.).

### **3. Project impact:**

- Ability of the program to meet the research challenges of the chosen scientific area;
- Economic and societal impact, contribution to the development of solutions in response to the challenges of the priority areas of the National Strategy;
- Strategy for dissemination (in itinere and ex post) and valorization of results, adherence to FAIR principles, Open Science and promotion of scientific culture.

## **4. General financing arrangements**

### **4.1. Funding**

PEPR-funded calls are exceptional in nature, and differ from recurrent funding for academic or research establishments.

The funds allocated represent additional resources for new initiatives. They can be used to launch innovative research projects, and finance, for example, the purchase of equipment, as well as personnel and operating expenses specifically assigned to these projects.

The consortium coordinator is responsible for allocating the budget among the participating teams.

Eligible expenses are specified in the PEPR financial regulations. Financial support will be provided in the form of a grant, to be disbursed by the ANR to the project coordinating institution, in accordance with the schedule set out in the contract, over the duration of the project.

### **4.2. Commitment letters**

In accordance with the model to be provided by Inserm, a letter of commitment will be signed between the coordinating Institution and the partner Institutions, specifying the rights and obligations of each Institution with regard to the implementation of the project. This letter of commitment must be provided by the coordinating Institution within a maximum period of 12 months from the date of signature of the contract awarding the grant.

All partner institutions allocating resources to the project are signatories to the letter of commitment, even if they do not receive a share of the grant.

## 4.3. Open science

As part of the ANR's contribution to the promotion and implementation of open science, and in line with the French National Plan for Open Science (PNZO) and the international Plan S, recipients of the France 2030 grant undertake to guarantee immediate open access to peer-reviewed scientific publications, and to adopt an approach to research data known as FAIR (Findable, Accessible, Interoperable, Reusable) in line with the principle of "as open as possible, as closed as necessary". Accordingly, all scientific publications resulting from projects funded under the PEPR program will be made freely available under the Creative Commons CC-BY or equivalent license, using one of the following three routes:

- publication in a natively open-access journal;
- publication in a subscription journal that is part of a so-called transforming agreement or transforming journal<sup>1</sup>;
- publication in a subscription journal. The publisher's version or the manuscript accepted for publication will be deposited in the HAL open archive by the authors under a CC- BY license, implementing the Non-assignment of Rights Strategy (SNCD), in accordance with the terms and conditions specified in the funding decision or contract.

In addition, the coordinating Institution undertakes to deposit the full text of these scientific publications (version accepted for publication or editor's version) in the national open archive HAL, at the latest at the time of publication, and to mention the ANR reference of the research project from which they originate.

The ANR encourages pre-prints to be deposited in open platforms or open archives, and to use permanent or unique identifiers (DOI or HAL Id, for example). The ANR also recommends that preference be given to publication in journals or books that are natively open access<sup>2</sup>.

Lastly, the coordinating institution undertakes to provide a first version of the Data Management Plan (DMP) within 6 months of the start of the program, in accordance with the procedures set out in the contract awarding the grant.

# 5. Submission procedure

## 5.1. Contents of the submission file

The submission file must include all the elements required for the scientific and technical evaluation of the project. It must be submitted by the closing date and time indicated on page 2.

**Important**

No additional information will be accepted after the closing date and time indicated on page 2.

The file must be submitted on the submission site, the address of which is given on page 2. In order to access this service, you must first obtain an account (login and password). We recommend that you register as soon as possible.

The complete submission file consists of a technical document written in English, including a description of the planned project in the format provided, a list of the ten best scientific publications by the teams involved, and short CVs of the principal investigators. The document must be converted into an unprotected pdf for submission.

The technical document template can be accessed from the publication page of this call for applications (see address on page 2).

## 5.2. Submission procedure

The documents in the submission file must be sent by the project manager:

**IN ELECTRONIC FORM imperatively:**

- before the closing date indicated on page 2 of this call for applications,
- on the submission website according to the recommendations on page 2.

Prior registration on the submission website is required to submit a project.

Only the electronic version of submission documents present on the submission site at the close of the call for applications will be taken into account for evaluation.

<sup>1</sup> Definition of [transforming agreement](https://www.coalition-s.org/faq-theme/publication-fees-costs-prices-business-models/) or [transforming journal](https://www.coalition-s.org/faq-theme/publication-fees-costs-prices-business-models/): <https://www.coalition-s.org/faq-theme/publication-fees-costs-prices-business-models/>

<sup>2</sup> The DOAJ site (<https://doaj.org/>) lists peer-reviewed, open-access scientific journals. The DOAB site (<https://www.doabooks.org/>) does the same for monographs.

An electronic acknowledgement of receipt will be sent to the project manager when the documents are submitted.

### **5.3. Submission tips**

We strongly recommend that you:

- open an account on the submission site as soon as possible;
- do not wait for the project submission deadline before entering data online and uploading files (note: it is imperative to respect the submission deadline);
- check that the document submitted in the dedicated "submission documents" area is complete and corresponds to the expected elements;
- regularly consult the program's dedicated website, at the address indicated on page 2, for up-to-date information on the program;
- consult the list of Frequently Asked Questions (FAQ) available on the website;

if necessary, contact the correspondents by e-mail at the address given on page 2 of this document.



**Contact: [equipe@pepr-sante-femmes-et-couples.fr](mailto:equipe@pepr-sante-femmes-et-couples.fr)**

**Project Manager: Eléna Gonçalves  
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