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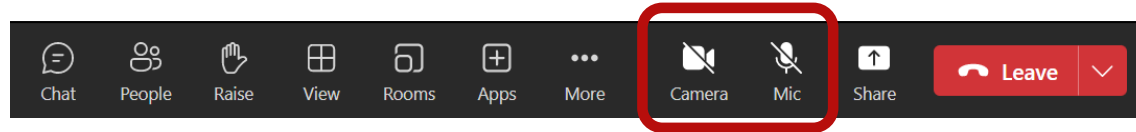
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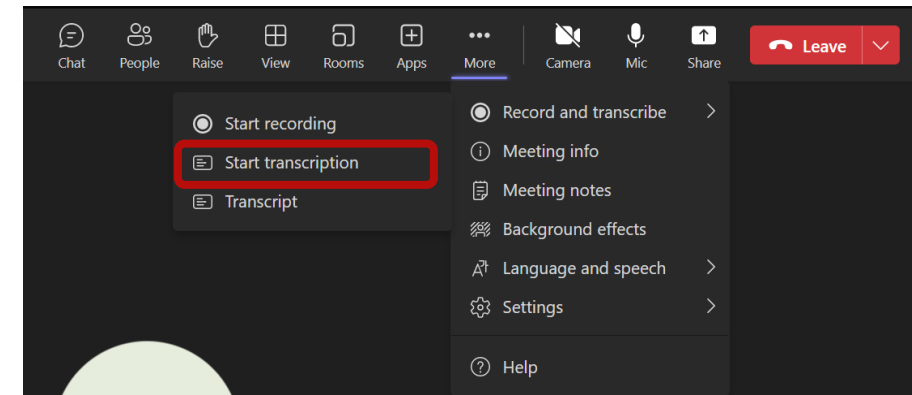
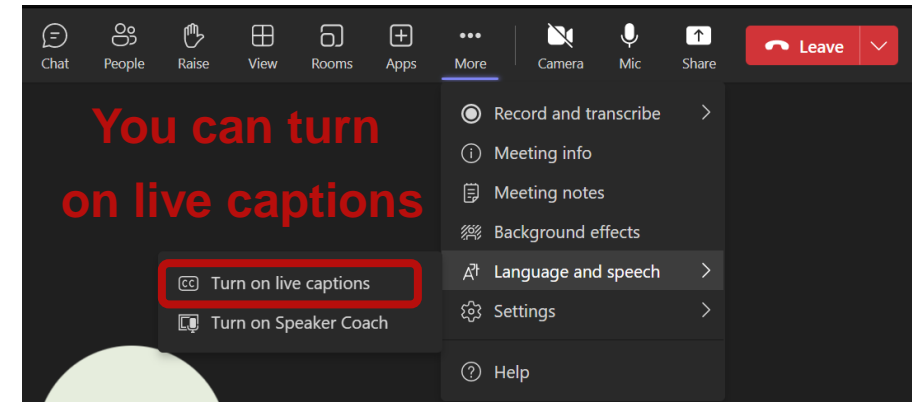
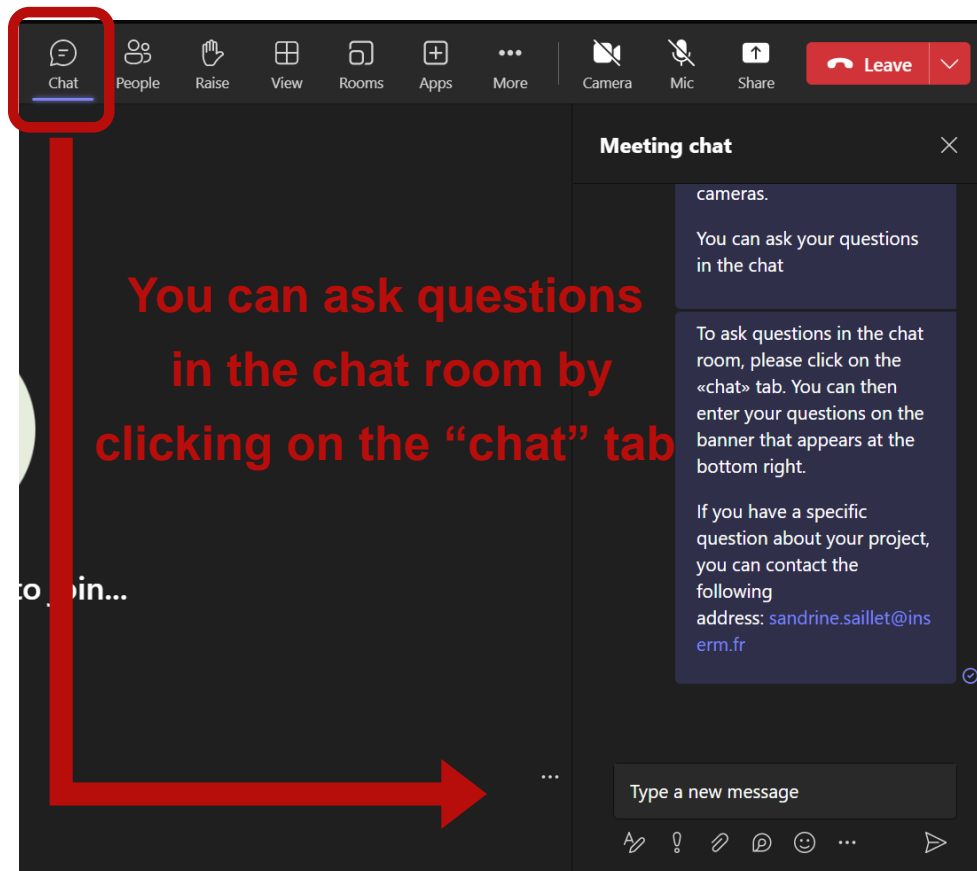
Antiepileptic Programme information webinar

March 16th 2023, 10-11:30 am (Paris time)

During the webinar



Your audio and video are turned off



You can have a live transcription, the text appears alongside the meeting video or audio in real time

Agenda



Context and challenge *10:00-10:30am*

- IReSP presentation by Rémy Slama
- MoH presentation by Chantal Guilhaume

Antiepileptic programme presentation *10:30-10:45 am*

- Call for Research Projects (research areas and objectives)
- Call for Expression of Interest (research area and objectives)

Support details *10:45 -11:00 am*

- Call for Research Projects
- Call for Expression of Interest

Questions *11:00-11:30 am*



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French Institute for Public Health Research

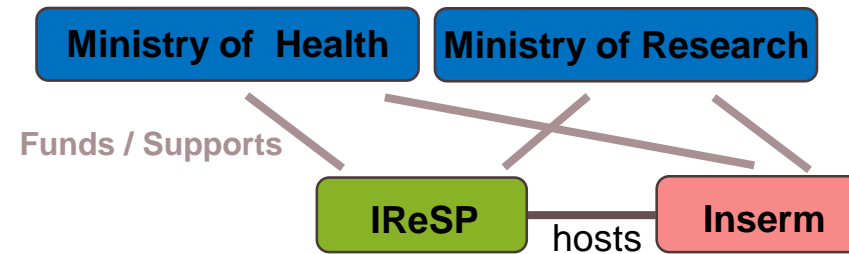
Rémy Slama, IReSP Director

French Institute for Public Health Research (IReSP)



IReSP:

Consortium with 12 members (Ministry of Health, Ministry of Research, National Health Insurance, Research Organisations, etc..) hosted by Inserm. Founded in 2007



Mission:

Develop and promote research in the field of public health:

- by acting at the interface between various actors in the field
- in relation to the knowledge needs of its members, and more broadly, of various actors involved and society as a whole

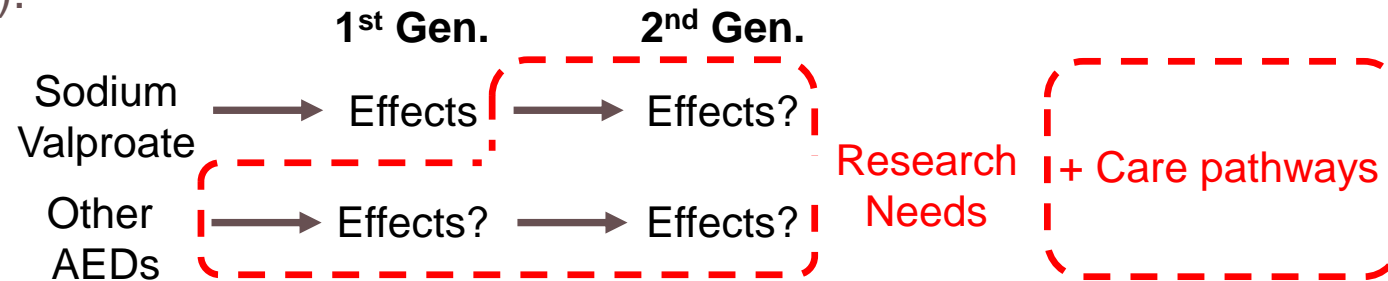


Research support programme background



Scientific question:

Short and long-term effects of *in utero* exposure to sodium valproate and other antiseizure medications (ASMs).



Four research priorities identified:

1. Teratogenicity and effects of ASMs on children exposed *in utero*.
2. Transgenerational effects of ASMs.
3. Toxicity mechanisms of ASMs.
4. Care pathways and inequalities in care access.

Financial support:

- 5 M€ euros from MoH, supporting research projects and communities (5 years)



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French Ministry of Health and Prevention

Chantal Guilhaume, DGS Head of the Medicines Office

Direction Générale de la Santé (DGS) Missions



Prepare public health policy and contribute to its implementation

- Developing, guiding and anchoring health policy
 - Define and implement strategies to improve health behaviours and living environments
 - Set the legislative and regulatory framework and develop and implement public health plans and national health programmes.
- Protecting populations
 - Ensure the capacity of the health system to detect, analyze and manage alerts and exceptional health situations
- Guaranteeing ethics, transparency and access to quality care for all
- Coordinate, lead, drive
 - Various partners: national and regional agencies, associations...

Risk associated to Antiepileptic drugs during pregnancy



- The French regulatory agency alerted on the risk of malformations and neurodevelopmental disorders associated with antiepileptic drugs during pregnancy and the need for further research in this area.
- The director general of health commissioned INSERM to propose a research programme on the effects of *in utero* exposure to sodium valproate and other anti-epileptic drugs with the following objectives.
 1. To identify the scientific issues relating to the health risks of *in utero* exposure to sodium valproate and other anti-epileptics;
 2. To prioritise these issues in order to highlight the priority area(s) of investigation;
 3. To Identify for each priority area the best way to address it (the study design and the necessary sizing).

A research programme to complement ongoing monitoring data



- Ongoing Studies based on exhaustive data from the National Health Data System (SNDS)
 - to estimate the risk of neurodevelopmental disorders among children exposed in utero to valproic acid indicated for epilepsy in France compared to unexposed children
 - to provide information on the characterisation of the risk of neurodevelopmental disorders associated with epilepsy treatments depending on the dose and the period of exposure during pregnancy
 - 2 reports available but additional analysis ongoing (New report to be published Q2 2023 [Actualité - Antiépileptiques au cours de la grossesse : Etat actuel des connaissances sur les risques de malformations et de troubles neuro-développementaux - ANSM \(sante.fr\)](#)).

A research programme to complement ongoing monitoring data



- Four research areas identified to guide DGS activities:
 1. Teratogenicity and effects of anti-epileptic drugs on child development
 2. Transgenerational effects of sodium valproate and other anti-epileptics
 3. Mechanisms of action of anti-epileptic drug toxicity
 4. Care pathways and inequalities in access to care for women with epilepsy and children exposed *in utero* to anti-epileptic drugs



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Antiepileptic Programme (two calls)

Sandrine Saillet, PhD IReSP Mission coordinator

Antiepileptic Programme



Scientific question:

Further explore short and long-term effects of *in utero* exposure to ASMs.

Two calls to address the research priorities:

➤ One Call for Research Projects:

Area 1: Teratogenic and developmental effects of ASMs in children exposed *in utero* (humans).

Area 2: Generational effects of ASMs (animals & humans).

Area 3: Toxicity mechanisms of ASMs in the context of *in utero* exposure (animals & humans).

Area 4: Care pathways and inequalities in care access for women women treated with antiseizure medications and children exposed *in utero* (humans).

➤ One Call for Expression of Interest:

Area: Intergenerational effects of ASMs on humans.

<https://iresp.net/financements/programmes-et-appels/programme-antiepileptiques/>

Call for Research Projects : Area 1



Fund selected advanced projects and pilot projects on the following area:

Research Area 1:

To improve the quantification and characterisation of the risks of birth defects and neurodevelopmental disorders associated with ASMs (commonly used during pregnancy) used alone or in combination.

Epidemiological studies from:

Medical, administrative databases, and existing databases on large populations (from hospitals, warehouses, medico-social facilities, registries, or other existing data sources).

- Priority will be given to projects relying on alternative approaches and sources than the sole SNDS.

Call for Research Projects : Area 2



Fund selected advanced projects and pilot projects on the following area:

Research Area 2:

To evaluate the generational risk of birth defects and neurodevelopmental disorders following *in utero* exposure to ASMs.

Animal studies:

Exposition of critical periods of gestation (compared to humans), to assess inter (F0, F1, F2) and transgenerational (F3) impact of ASMs. Physiology and pathology in young and older adults, assessment (gonads, reproductive tract and kidney etc.), neurological testing (anxiety, memory, etc.).

Epidemiological studies:

In children and grandchildren of women exposed to ASMs during pregnancy, to assess pathologies (non-exposed and exposed populations) in young adults and/or older adults.

Call for Research Projects : Area 3



Fund selected advanced projects and pilot projects on the following area:

Research Area 3:

To establish the cellular and molecular mechanisms by which the most commonly used ASMs in pregnancy are likely to disrupt organogenesis and development or induce specific diseases.

Animal studies:

Comparative studies of different ASMs and *in utero* exposure at different periods of time during development. Purified cell populations to screen mechanisms, downstream transcriptional events, and classic toxicology screens for the different ASMs.

Human studies:

Purified cell populations of placental tissue (trophoblasts) and embryonic tissue (skin) to study impacts on gene expression and epigenetics (DNA methylation). Epigenetic programming to assess long-term developmental impacts on the individual later in life. Measures in the adults to assess cognition and social interactions.

Call for Research Projects : Area 4



Fund selected advanced projects and pilot projects on the following area:

Research Area 4:

To analyse the existing care pathways and inequalities in care access of epileptic women and children exposed to ASMs *in utero* (social or geographic), the crucial period of transition (adolescence to adulthood in women), knowledge/practices (practitioners and patients), and ethical issues (pregnancy risks) associated.

Human studies:

Data collected for research (cohorts/randomised trials) matched with SNDS, practice studies, longitudinal approaches, qualitative studies (patients and healthcare professionals) and interventional research.

Call for Expression of Interest



Two-step process:

First: allow to identify and select complementary research teams, to second: support them in the co-construction of a research project that may be funded after evaluation.

Research Area:

To develop an epidemiological study to assess the intergenerational effects of ASMs in children and grandchildren of mothers exposed to antiseizure medications during pregnancy.

Human study:

Develop an epidemiological study in populations to assess the intergenerational risk in children and grandchildren born to mothers exposed to ASMs during pregnancy, based on existing data or data not yet or only partly gathered (e.g., records of medications used in pregnancy, maternal indication for use of ASMs, maternal comorbidity, etc.), covering a long enough time period, allowing to providing an accurate assessment of the use of ASMs.



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Calls details

<https://iresp.net/financements/programmes-et-appels/programme-antiepileptiques/>

Call for Research Projects (CRP)



Agenda:

- Deadline for electronic submission: May 24th, 2023 - 3 p.m. (Paris time) <https://www.eva3.inserm.fr/>
- Scientific Evaluations: June to November 2023
- Announcement: December 2023

Support modalities:

Complete Research Projects

- Duration: up to 36 months
- Budget: €40,000 to €800,000

Pilot Research Projects

- Duration: 12 to 24 months
- Budget: up to 100,000 maximum

Call Launch
Feb 20th, 2023

Deadline
May 24th, 2023

Results Publication
December 2023

CRP Applications

CRP Evaluations

Webinar
March 16th, 2023

Scientific evaluations
June to November 2023

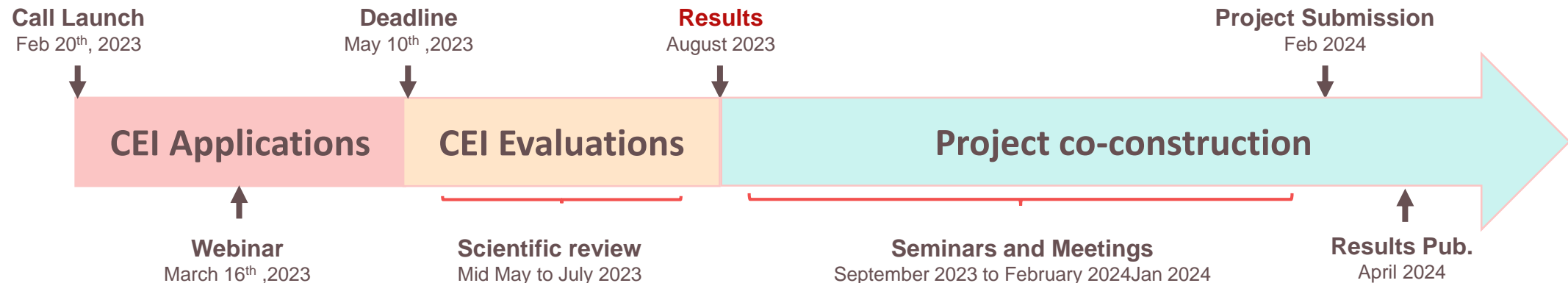


Call for Expression of Interest (CEI)



Agenda:

- Deadline for electronic submission : May 10th, 2023 - 3 p.m. (Paris time) <https://www.eva3.inserm.fr/>
- Scientific Evaluation: Mid-May to July 2023
- Announcement: August 2023
- Co-construction (seminars and meetings): Sep 2023 to Feb 2024
- Project Submission: February 2024
- Results publication: April 2024





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Questions

Sandrine Saillet, PhD IReSP Mission coordinator

Where can I find the full information on both calls?



Full information is available on IReSP website:

<https://iresp.net/financements/programmes-et-appels/programme-antiepileptiques/>

Antiepileptic Programme page gives access to both calls:

- Call for Research Project :
 - Texts call (French & English version)
 - Application form (word file) and budgetary appendix (excel file)
- Call for Expression of Interest :
 - Texts call (French & English version)
 - Application form (word file) only

Can I apply for both calls?



The antiepileptic programme is composed of two different but related calls.

It is possible to apply for the call for research project and for the call for expression of interest. However, projects must be distinct and address different research (areas) in line with the research dimension of the calls and with the appropriate research ambitions.

Call for Research Project

- Is a one step process that will provide financial support for selected research projects.

Call for Expression of Interest

- Is a two step process that will:
 1. Allow to identify and select teams with complementarity expertise (step one).
 2. Selected teams, with the support of IReSP, will co-construct a research project that will then be evaluated for funding (step two).

Applications conditions



To be eligible for the Call for Research Project:

- Affiliated organisations of the scientific coordinator and team leaders of **must be eligible organisations**;
- Scientific coordinators **must be French residents and belong to a French organisation**;
- Partner teams must belong to eligible affiliated organisation;
- Non-French teams can apply for funding. However non-French teams will be funded at a maximum of 35% of the total amount of funding requested.

To be eligible for the Call for expression of interest:

- The affiliated organisations of candidates **must be eligible organisations**;
- Non–French teams can apply.

How can I apply?



Electronic submission only on EVA 3 : <https://www.eva3.inserm.fr/>

Call for Research Project (deadline May 24th , 2023 -3 p.m. Paris time)

- Fill the form
- Download 2 documents:
 - Application form (word format)
 - Budgetary appendix (excel format)

Call for expression of interest (deadline May 10th , 2023 -3 p.m. Paris time)

- Fill the form
- Download the application form (word format) only

Can foreign researchers participate?



Call for Research Project

Foreign teams can apply for funding only if they are coordinated and associated with a French team as partner teams. However, they will be funded at max. 35% of the total amount of the funding requested.

Note: Projects involving foreign teams will be looked carefully, regarding the added value provided by these teams.

Call for expression of interest

Foreign teams can apply for the co-construction.



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Thank you for your attention!