PERINAT COLLECTION®

PLATFORM CHARTER

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DEFINITIONS

The Perinat Collection ® Platform: (hereinafter Perinat) is a trademarked data biobank containing essential foetal and perinatal biological collections, mother-child clinical data and ultrasounds of the mother and foetus.

The PremUp Foundation: The PremUp Foundation was founded in France in 2007 and is the only Thematic Research and Healthcare Network (RTRS in French) exclusively for perinatal care. Public authorities started this scientific cooperation foundation to support multidisciplinary projects that currently bring together top medical and health research institutions in perinatal care, including maternity units, type III neonatal services and leading research units.

The PremUp R&D Team: The foundation's unit that coordinates research and development projects in line with its missions. It is comprised of a project director who is a Perinat manager and a member of the PremUp management team.

Clinical data and digitised imagery: Clinical data on mothers and children in neonatal care and ultrasound data are logged into the same computer system and stored anonymously on a server

Bioresources or Biological Resources: The biological resources contain biological materials along with clinical data on patients and technical data on samples. It is essential to pair biological material with its related data in order to use the collections properly and produce quality research.

Users: Any academic, industrial or other types of research teams that have submitted a request to the special committee (advisory or scientific committee) to access Perinat's data or bioresources stating how they plan to use them and which have obtained written permission, subject to third-party rights.

Partners: Perinat's mission is to increase interactions with national, European and international clinical research teams. These teams work at hospital units, clinical investigation centres, analysis platforms, biotech startups, pharmaceutical/cosmetics companies and medical instrumentation companies.

Contributors: A person or entity providing Perinat clinical data or bioresources.

Advisory Committee: Comprised of two PremUp team members (management or R&D team). This committee is consulted for requests to access only the clinical data and/or digitised imagery. It connects users and provides information for completed or ongoing studies.

Scientific Committee: Comprised of a representative specialised in each discipline (neonatal care, obstetrics, imaging, biology) and a PremUp team member (management or R&D team) sitting on the PremUp Executive Board. It is consulted for requests to use bioresources in the Perinat collection.

Ethics Committee: It is composed of five leading French or foreign figures, external to the Foundation.

The MTA: The MTA (Material Transfer Agreement) or user's licence.

This is a contract whereby the organisation that owns the material grants a partner a non-exclusive right to use said findings, model, biological instrument, etc. for the purposes of specific research as indicated in the partner's request.

1) ABOUT PERINAT

Perinat comprises:

- A **collection of prenatal mother-child biological samples**: serum, DNA, amniotic fluid, etc. that is centrally hosted at the NFS96-900 certified Biological Resource Centre of the Créteil Intercommunal Hospital Centre (CRB at the CHIC) or a similar centre contracted by the PremUp Foundation.
- A **collection of cellular tissue and biological samples specifically from placentas**, held centrally on the PremUp Placentech® platform.
- A **collection of tissue and cell samples specifically from the brains** of deceased foetuses and newborn babies held centrally at the Robert Debré Hospital foetopathology laboratory.
- **These laboratories uphold regulated standards on traceability and quality.**
- A **collection of clinical data** from pregnant women and newborn babies, specifically those born prematurely.
- A **collection of ultrasound images** from pregnant women.

2) ACCESS TO THE DIGITISED AND BIOLOGICAL RESOURCES

a) Request for bioresources and related data

- People or organisations in the PremUp network looking to access Perinat resources (clinical data or bioresources, samples, cells or tissue) must submit a detailed written request on the platform. This request is automatically forwarded to the Perinat administrator, who sends it as required to the Scientific Committee to be approved or denied.
- People or organisations not in the network (referred to as "the requesting party") looking to conduct research must submit their detailed written request to the PremUp R&D team which does a feasibility review. Depending on the outcome, the PremUp R&D team forwards the request to the Scientific Committee or replies to the

requesting party directly if the research cannot be done with those resources. The person or organisation can then resubmit and send back the request.

In either case, an online application form must be completed on the Perinat website.

It specifies:

- The name of the person managing the project, status, organisation, clinical department or research unit and staff members.
- The project's name and detailed content.
- The biological samples requested and the quantity needed to conduct the project.
- The clinical selection criteria for subjects and any helpful related clinical data.
- Any special requests for preparation and/or conservation.
- The purpose and expected findings of the study.

b) Review process for requests from teams inside or outside the network

i) Request

- Requests are forwarded to the PremUp R&D team.
- The PremUp R&D team verifies the admissibility of requests and the time it will take to obtain samples. A confirmation of receipt is sent to the requesting party.
- An email is sent to the Scientific Committee along with PremUp's recommendation. It reviews the scientific potential and the ethical/regulatory considerations of the request. It uses a standardised form to conduct its review.
- PremUp then emails a reply (containing the Scientific Committee's review, if applicable) to the requesting party within three weeks from when the request was submitted. Reasons are provided if the request is denied.

ii) Review

If any ethical or regulatory issues arise during the initial review process, the matter is referred to the competent bodies, including the PremUp Ethics Committee, but only if the initial scientific review is positive.

iii) Reply

- Once the request is approved, samples are provided when the terms of the contract are met and any sort of agreements are signed for a collaboration, service, MTA, etc.
- Clinical or research units inside the network may only submit up to two research projects at a time and are not permitted to file a new request until one of those projects has resulted in a manuscript submitted for publication or proof is provided that the project has been shelved.
- Except in special cases that have been discussed with the Scientific Committee, at least one year must pass before submitting another project for review. If two or more clinical/research units wish to work on the same subject, they are asked to combine their projects.
- Any clinical/research unit may deny permission to forward and/or use its data for a project conducted by another unit, but they must specify the basis for this denial with the Scientific Committee.
- Prior to being presented to the Scientific Committee, scientific projects must first be validated by the Clinical Research Unit or a reputable independent consultant.

3) ACCESS TO ONLY CLINICAL DATA AND/OR DIGITISED IMAGERY

The request is forwarded to the Advisory Committee which puts the requesting party in contact with the teams that have provided the data. Any clinical/research unit may deny permission to forward and/or use its data for a project conducted by another unit, but they must then specify the basis for this denial with the Advisory Committee, which sends it to the requesting party.

4) RULES ON SAFE AND PROPER USE

a) For users

- Users agree not to use samples for any other purposes than those indicated in the request form submitted (open collection). They also undertake not to sell digitised or biological resources to any other person or organisation without consent from the PremUp team.
- Users of the platform agree to open a login session with their own username and password and to not disclose this information.
- When the research is complete, they agree to dispose of any remaining samples in accordance with the terms stated when their request is approved.
- Users undertake to follow the publication rules set forth in this document.

b) For contributors

- If all the procedures are not completed prior to the request for bioresources (e.g. statement of conservation of human biological samples for research purposes from the organisation hosting the requesting party, etc.), a request will also be made for an agreement to comply with regulations in force.
- Contributors must verify with their organisation that current regulations are being followed, specifically but not limited to filing the research protocol with the competent authorities and donor consent form (or a non-objection form) each time these documents are required. They then send the resulting recommendations or authorisations to the PremUp R&D team.
- When required, contributors must update the platform with any changes to or termination of the research protocol as well as any information on the availability of collections and terms of access.
- Contributors undertake to contact the laboratory in question to arrange conservation methods for those samples before the collection is compiled or prior to it being submitted.
- They must also oversee any transfer procedures for both computer data and biological resources.

- Contributors agree to provide all available information. The data cannot be sorted or filtered.
- Only the project's original contributor may be given access to a submitted collection in accordance with the procedures agreed upon jointly when the request is approved. Once the research is complete, the submitter may opt to recover any unused samples, let Perinat handle the matter subject to specific terms on the right of Perinat or its employees to examine or access them, or to give them to Perinat, and this in compliance with the terms set forth in the protocol.
- Contributors only see their original institution's computer data inside Perinat. They must submit a data request to the PremUp R&D team to access other Perinat data.
- A contract between PremUp and the contributor (or its host organisation) stipulates all the procedures for incorporating these computer data and/or samples in Perinat and exporting, using and developing them. Contributors undertake to follow Perinat's publication rules.

c) PremUp as a Perinat project originator

With regard to research teams, PremUp agrees to abide by all applicable confidentiality rules when the request is submitted, followed up and carried out.

PremUp undertakes to provide the samples and related clinical data in accordance with the protocols and consent granted by each participating subject. It ensures compliance with embargo and priority rules. It undertakes to oversee the entire traceability chain for samples and to vouch for its quality.

- In closed collections, preserved samples may be briefly indicated (quantity, type of sample and pathology only) in the biobank catalogue, unless the contributor has a specific objection.
- In open collections, Perinat agrees to comply with the rules in this document and the priority rules agreed upon when the project is written and/or the contract is signed and to consult the Scientific Committee and follow its recommendations if any conflicts of interest arise.

- PremUp shall inspect or ask the contributor to inspect that the data are not altered in any way or willingly/accidentally destroyed while being processed, stored or transferred and that they remain in a useable format.

d) Publication rules

All contributors and users of samples sent via the platform must **cite Perinat's contribution** in any written publications (including online publications) or when verbally disclosing project findings resulting from the use of any bioresources provided and/or managed on the platform and/or clinical data, at a minimum in the Materials and Methods section, if not as a co-author if one or more members of the platform was heavily involved in the project.

Any publication produced by using Perinat's biological resources contractually managed by the Biological Resource Centre (CRB) of the Créteil Intercommunal Hospital Centre (CHIC) or any similar centre contracted by PremUp cites it in the acknowledgements.

Contributors and users of samples from the Perinat Collection also undertake to comply with the intellectual property rules.

Distribution of research findings. PremUp requires that its customers ensure the identity of participants remain anonymous (unless prior consent has been granted) when distributing any findings obtained by using the biological material.

e) Feedback

A copy of any publications made possible by using the samples shall always be sent to the PremUp R&D team so that the platform can support the legitimacy of its activity with its stakeholders (the ANR and others) and for the purposes of posting the findings on the Perinat and PremUp websites.

5) TERMS OF CONFIDENTIALITY

The ethical duty of confidentiality refers to the obligation that binds persons and organisations to protect the information entrusted in them. This duty includes the obligation to prevent the information from unauthorised access, use, disclosure and alteration as well

as from being lost or stolen. It is imperative to carry out this ethical duty of confidentiality in order to uphold the bond of trust between researcher and participant as much as the integrity of the research project.

Anyone attending a Perinat meeting is bound to keep all information divulged during these sessions in the strictest confidentiality: meeting minutes and any information from these documents as well as other presentations made in these meetings. This rule shall be systematically stated on the meeting attendance sheet, which serves as a written disclaimer upon signing. In some cases, this consent may be additionally formalised by signing a special document.

Representatives of pharmaceutical or medical instrumentation companies are strictly bound by this confidentiality rule. Terms and conditions authorising them to share specific information from Perinat meetings in their respective companies will have been stipulated in the contract binding them to PremUp for the research study in question.

6) RESTRICTION ON ACCESS TO THE BIOLOGICAL MATERIAL

Access to the biological material in the biobank as well as any related data is strictly reserved for people authorised by the PremUp R&D team. Access for undesignated third parties is strictly forbidden, with the exception of staff performing maintenance on the materials who must comply with the confidentiality rules set forth in the PremUp contract.

7) DESTRUCTION PROCEDURES

Confidentiality shall be upheld when destroying biological materials and the applicable standard safety procedures followed.

8) SCIENTIFIC RESPONSIBILITY AND INTEGRITY

Perinat, its users and partners ensure the responsible use of biological resources and the scientific integrity of their activities. User partners must exercise caution in disseminating their research findings.

9) INTELLECTUAL PROPERTY COMPLIANCE

PremUp, Perinat and its users and partners encourage the advancement of scientific and technical progress resulting from the collection, preservation and provision and use of biological resources for research purposes. The access to and use of biological resources are subject to written agreements between PremUp on the coordination of research projects conducted within the scope of Perinat and its partners or users that, specifically, cover practices pertaining to partnerships, promotion and intellectual property. Without prejudice to any intellectual property rights, PremUp, the PremUp network and its partners agree to redistribute the societal benefits and values of the research conducted using the biological resources provided through Perinat ***(Intellectual Property Code - Consolidated Version of 8 August 2015).***

10) APPLICATIONS

This charter applies to all of Perinat's users, partners, employees and contributors.

Perinat, its users and partners generally comply with the legislation and best practices applicable to their field.

11) MEASURES TAKEN IF THE CHARTER IS VIOLATED

Any violation of a provision in this charter committed by a signatory shall result in that signatory being promptly banned from the network and all collaboration ceased with the Perinat Platform. PremUp shall provide written notification of such a ban.

Anyone banned as well as any partner or user involved shall be blocked from the website and all input interfaces developed by PremUp.

Users are personally responsible for failure to comply with the legal provisions and any principles stated or repeated in the charter.

I, undersigned,…… certify that I have understood this charter and undertake to comply with it.

Date: ……..

Signature:

Surname and Position in the company or academic institution:……..

APPENDIX 1: APPLICABLE LEGISLATION AND BEST PRACTICES

Public Health Act: Act No. 2004-806 of 9 August 2004. Replaces Act No. 88-1138 of 20 December 1988 as modified, the so-called Huriet-Sérusclat Act pertaining to the protection of persons consenting to biomedical research. Circular No. DGS/SD1C/2005/123 of 7 March 2005 pertaining to the entry into force of provisions on biomedical research resulting from Act No. 2004-806 of 9 August 2004.

European Directive: Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

CNIL: Computing and Freedom Act No. 78-17 of 6 January 1978 as modified by acts No. 94-548 of 1 July 1994, No. 2002-303 of 4 March 2002 and No. 2004-801 of 6 August 2004 on the protection of physical persons in the treatment of personal data.

Bioethics Laws: Acts No. 94-653 and No. 94-654 of 29 July 1994 pertaining to the donation and use of human elements and products, medical assistance, procreation and prenatal diagnostics. Act No. 2004-800 of 6 August 2004 on collecting human biological samples.

Good Clinical Practices: These are "the set of requirements which must be observed for designing, conducting, recording and reporting clinical trials that involve medication to provide assurance that the results are credible, the rights and safety of trial subjects are protected and their information is kept confidential." The decision titled “Good Clinical Practices (GCP) for Biomedical Research on Medication for Human Consumption” of 24 November 2006 was published in the Official Gazette of 30 November 2006. This GCP Decision is currently the standard in France and replaces the good clinical practices published in Official Gazette No. 87-32bis.

ICH (International Conference on Harmonisation): Conferences held in Europe, Japan and the United States to harmonise clinical trial recommendations.

The Declaration of Helsinki: Established by the World Medical Association (WMA) as a set of ethical principles regarding medical research on humans, including research on human biomedical material and identifiable data.