CRBIP CHARTER ON MANAGEMENT OF BIOLOGICAL RESOURCES

The Institut Pasteur has set up a Biological Resource Center (CRBIP) that follows the principles described in this Charter.

The CRBIP:

- preserves and provides access to microbial and human-origin biological resources (biospecimens and associated data) and biospecimen-related services, including hosting of collections, laboratory processing, quality control and characterization of samples.
- supports research and research applications serving or collaborating with partners from both the public and private sectors.
- serves in priority Institut Pasteur scientists and scientists working on human diseases and/or public health.

The fundamental **principles** governing the CRBIP are custodianship of the biological resources based on our responsibility for their quality, confidentiality around donor-related data, impartiality based on absence of scientific or financial conflict of interest in any decision making, transparency in our policies and procedures, service ethos.
We also support open science, based on the principle “as open as possible, as close as necessary”.

The CRBIP is a research infrastructure. Our **policy on research activities** supports (i) internal polyphasic taxonomic research, which includes both genomic and phenotypic taxonomic traits and corresponding, existing or innovative, bioinformatics tools, (ii) biospecimen research, which includes experimental or bioinformatic method validation and/or stability studies. The overarching objective of all research we may be performing is to improve the quality of the collections we are preserving. We may exceptionally be participating in discovery research contributing experimental or bioinformatic work in particular areas of our expertise; in this context, the CRBIP expects a co-authorship in the scientific publications. Simple distribution of biological resources is not considered as research activity per se; in this context, the CRBIP expects an acknowledgment in scientific publications.

Our **quality policy** supports accreditation to ISO20387 of the biobank laboratories for CRBIP units that may be distributing biological resources to industrial partners or that may be involved in clinical or diagnostic research projects. Certification to ISO9001 is deemed sufficient for CRBIP units that either do not distribute biological resources to third parties or distribute biological resources to end-users who do not require accreditation or that are using difficult-to-validate processing methods.

From a regulatory point of view, we are compliant to all applicable national and international **regulations**, based on the following policies:

- In the area of data management:
  - <u>for microbial collections</u>,
    - depositor personal data are maintained for the period of availability of the biological material, prolonged by 99 years, and communicated via the database;
    - end user data are kept also for the period of availability of the biological material, prolonged by 99 years for customer satisfaction surveys, market surveillance, and traceability purposes;
    - associated data are metadata, and analytical characterisation data including sequencing data. Metadata are part of our open catalogue and shared with European and international catalogues and databases (MIRRI, GCM, BacDive). Analytical data can be shared with

end users upon request and can be made publicly available upon approval by our Steering Committee.

NOTE. The Bacterial Diversity Metadatabase BacDive is the worldwide largest database for standardized bacterial phenotypic information. Its mission is to mobilize research data on strain level from internal files in culture collections (e.g. CABI, CIP, CCUG, DSMZ) as well as from primary literature and make it freely accessible.

- For human origin collections,
  - associated data are of three types: basic demographic, clinical/ biological, preanalytical/logistical. Data are pseudonymised. "Collection projects" are implemented, in collaboration with the Clinical Investigation Unit, to maximise use of biological resources in different research projects, hence data are kept and are made available to approved research projects until samples are exhausted. Dynamic information on the Institut Pasteur website (research.pasteur.fr) and on the CRBIP website (www.crbip.pasteur.fr) allows donors to be informed on the types of research projects using CRBIP samples.
  - In an effort towards maximization of the secondary usages of biospecimen collections of human origin, the CRBIP may communicate to potentially interested Pasteurian researchers on the existence of relevant collections, even when these collections are not part of the public catalogue. In such cases, the PI of the collection is the sole decision maker, providing access, or not, to the collection.

- In the area of research involving human specimens: we proceed to all necessary declarations and authorisation requests from the French Ministry of Higher Education and Research. Our processes and procedures ensure close collaboration with the Institut Pasteur Medical Department, Legal Department, and Institutional Review Board, thus ensuring that all necessary approvals from ethics committees and/or data protection agencies are obtained.
- In the area of the Nagoya Protocol (NP): we do due diligence for all prospectively acquired strains. We provide all available information, for both prospectively acquired and historical strains, to end users of microbial strains. We do not consider genomic data of strains to be in the scope of NP, except if the country of origin's ABS (Access and Benefit Sharing) regulations explicitly state otherwise. We consider isolated strains only to be in the scope of NP. Human-origin specimens (e.g. fecal samples) are not considered to be in the scope of NP, even if they may contain molecules (such as antibodies) that are produced as a specific immune response to a microorganism.
- In the area of Genetically Modified Organisms (GMO): we are compliant to all national regulations regarding management, biosecurity, and biosafety and hold the necessary authorisations of use of GMOs in confined environments for research, development and teaching purposes from the French Ministry of Higher Education and Research.

We ensure a regulatory watch in all the above areas.

- In the area of pricing, our **price policy** is summarized below

	Internal Institut Pasteur[1] end users	External academic or not for profit[2] end users	External private[3] end users	Users from French Educational Institutions[4]
Microbial biological resources	Minimum fees (CRBIP catalogue) Free for depositors	Fixed fees (CRBIP catalogue)[5]	Fixed fees (CRBIP catalogue), and DARRI* involvement in Material Transfer Agreement negotiation, if applicable	Minimum fees over microbial strains suitable for teaching purposes (CRBIP catalogue)
Human biological resources	Free (from stock)	International academic fees	Fees defined in agreement with DARRI*	Not applicable
Services other than storage	Cost calculation according to IP procedure, Internal IP fees (PPMS platform)	Cost calculation according to IP procedure, external academic fees	Cost calculation according to IP procedure (industrial fees) and DARRI* involvement in Service Agreement negotiation, if applicable	Not applicable
Storage services	Free, in the limit of available storage space	Fixed fees	Fixed fees	Not applicable

[1]Units of Institut Pasteur campus and secondary establishments (Institut Pasteur of Guyana, Institut Pasteur of Guadeloupe, Institut Pasteur of New Caledonia, Institut de l'Audition).
[2]Public or private organisations carrying out research activity; members of the Pasteur Network (except secondary establishments); Start-ups (commercial companies created to exploit the results of Institut Pasteur research); Bioaster.
[3]Commercial companies having an activity of production, manufacturing, and distribution of products on a market or service.
[4]Public or private French educational establishments providing training for French degrees, such as professional 'baccalauréat', BEP. BT, BTS or equivalent. This includes schools ('écoles'), 'lycées', colleges ('collèges), CFA ('Centre de Formation d'Apprentis'), IUT ('instituts universitaires de technologie'), professional training centres ('centres de formation professionnelle continue'), among others.
[5]Ad hoc price reductions can be applied to clients, especially those who have isolated strains in the context of public health surveillance, and agreed to their deposit by Institut Pasteur National Reference Centres.
*DARRI, Direction des Applications de la Recherche et des Relations Industrielles

Our **deposit and hosting policy** includes some restrictions:

- The CNCM, as an International Depositary Authority (IDA), applies restrictions for acquiring and storing biological resources in accordance with the Communication from the Government of the French Republic to the World Intellectual Property Organization (Budapest Notification No. 214) on the scale of fees collected in euros by the CNCM and on the kinds of microorganisms that may be deposited. The CNCM reserves the possibility of refusing any cell culture which, according to the curator, involves an unacceptable risk or is not suitable for handling due to technical reasons,

and any microorganism that may imply specific risks to human beings, animals, plants or the environment.

- The PCC applies technical restrictions, and only accepts deposits of axenic cyanobacteria.
- The CIP applies biological restrictions and does not accept deposits of "Microorganisms and Toxins" ("MOT")-status strains, according to the applicable French regulations.
- The CHIP applies biological restrictions and does not accept samples from patients known to be infected by "MOT"-status pathogens, except when collaborating with the CIBU (Cellule d'Intervention Biologique d'Urgence). The CHIP accepts collections after approval of the corresponding project by the CPS (Comite de Promotion et de Suivi).

Our **access policy** includes the possibility of an up to 5-year embargo for biological resources of human origin. Such embargo is decided by the Principal Investigator (PI) of the project-specific collection. Biological resources of human origin are distributed only following approval by an independent Sample Access Committee (SAC) that may set priorities according to technical, logistical, scientific and ethical criteria (*CRBIP_PM_PL_005_Charter CRBIP Sample Access Committee*). Microbial resources may be subject to a reasonable embargo period if a deposit is done before the corresponding manuscript is published. They are distributed for research, quality control or educational purposes, **without restriction** and according to our general terms and conditions of use ("CGTU"). Distribution for commercial purposes is possible for (i) all strains deposited before 1994, (ii) strains from 1995 onwards, for which the depositor has not objected to such use. Any known restrictions pursuant to the Nagoya Protocol are communicated to the end users. Distribution of a microbial resource to another microbial biobank can take place only in the context of the other biobank's internal research or quality control operations, and according to our general terms and conditions of use ("CGTU"). If another biobank requests a strain for re-distribution to its clients in the context of its biobanking operations, a specific contract can be negotiated.

Our **publication policy** is to request due acknowledgement in scientific publications making reference to CRBIP biological resources or their derivatives, (i) when CRBIP biological resources have been distributed from stock, (ii) when CRBIP biological resources have been collected and processed according to CRBIP standard operating procedures (SOPs), or (iii) when CRBIP biological resources have been collected and processed with experimental methods without prior formal method validation by CRBIP. We request co-authorship in scientific publications when CRBIP biological resources have been collected and processed with project-specific methods that have also been formally validated by CRBIP, or when specific analytical and/or bioinformatics work has been performed.

Our **"return of results" policy**: concerning any "incidental findings" from specimens of human origin, in the improbable case where CRBIP would encounter such findings, these would be communicated to the donor only if (i) they are actionable, (ii) the donor has agreed with such return of results, and (iii) only through a clinical / principal investigator.

Our **Intellectual Property (IP) policy**: CRBIP is the custodian of biological resources. CRBIP has no IP rights in inventions made by end users. However, a non-exclusive licence may be negotiated when commercial products based on CRBIP bioresources and/or expertise are developed.

Our policy in terms of collaboration with the **Pasteur Network** (PN) supports priority access to CRBIP biological resources, internships and common catalogue of collections. We believe processes and workflows according to which biological resources collected in a country of the PN remain in the country and are used in the country, should always be favoured. We also believe that common minimum datasets and harmonised SOPs (Standard Operating Procedures) can enhance the scientific value and utilisations of the biological resources across the PN and beyond.

The **governance** and oversight of CRBIP is based on an institutional Steering Committee (*CRBIP_PM_PL_002_Charter CRBIP Steering Committee*) and an external Scientific Advisory Board (*CRBIP_PM_PL_001_Charter CRBIP Scientific Advisory Board*). All potential scientific conflicts of interest are disclosed.