



General Terms CRYOSTEM Call for Projects 2017

These general terms (hereafter the “**General Terms**”) aim in particular to present the terms and conditions governing the submission, selection and processing of academic or commercial research projects submitted to CRYOSTEM Scientific Committee.

INTRODUCTION :

CRYOSTEM is a project that is backed by the SFGM-TC (Francophone Society for Bone Marrow Transplantations and Cell Therapy (hereafter “**SFGM-TC**”) and accepted by the French National Research Agency in relation to the “Cohorts” call for projects funded under the French government’s “National Investment Programme” (“*Investissements d’avenir*”) in June 2010.

Currently, CRYOSTEM is a network covering 33 of the 36 allo-transplantation centres in France and 23 related Biological Resource Centres (BRC).

Since 2012, CRYOSTEM has set up a collection of biological samples taken before and after allogeneic hematopoietic stem cell transplantation (HSCT) (hereafter the “**Collection**”), thus reaching its first objective.

Starting in April 2015, this Collection will be made available to scientists to enable high-level scientific projects to be performed focussing on the theme of Graft versus Host Disease (GvHD). The objective is to better understand the physiopathology of this little-known disease in humans, the predictive factors related to its occurrence, the response to immunosuppressive treatments and the long-term prognosis.

In 2016, CRYOSTEM obtained the authorization of the French Patient Protection Committee (CPP) to extend the collection thematic to the all HSCT complications, opening the fields of studies.

In relation to this availability, CRYOSTEM wishes to choose the most relevant scientific projects complying with the chosen scientific theme.

COORDINATEURS

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PART I – GENERAL TERMS

I.1 – Purpose of the Call for Projects

The purpose of this Call for Projects (hereafter “**Call for Projects**”) is to open up the access to the Collection, established by CRYOSTEM, to all academic and/or commercial members as defined in article I.2 below, involved in research on all the Hematopoietic Stem Cell Transplantation (HSCT) Complications, and who wish to work on the scientific themes identified by CRYOSTEM.

The projects (hereafter “**Projects**”) put forward by the academic and/or commercial members (hereafter “**Applicants**”) in relation to this Call for Projects must abide by these General Terms and the Appendices.

The Applicants acknowledge that they have read and accepted these General Terms and the Appendices, by signing the act of commitment of the General Terms that will be sent to them before samples delivery.

For this Call for Projects, the CryoStem “**Scientific Committee**” has defined the content of this Call for Projects and is responsible for organizing the selection process and follow-up of the Projects. Its members are listed in Appendix 1.

I.2 – Conditions for submitting replies to the Call for Projects

The Applicants involved in this Call for Projects are as follows:

- Academic laboratories such as those registered by the Ministry for Higher Education and Research or under the supervision of this same Ministry, i.e. any laboratory of the following structures: higher education and research establishments, public scientific establishments, public industrial and commercial establishments, public scientific and technological establishments, foundations, public interest groups, research organizations, regional delegations for research and technology (hereafter “**Academic Laboratories**”). The term “Academic Laboratories” in these General Terms includes consortiums and groups of laboratories of these same structures
- Commercial Applicants (hereafter “**Commercial Applicants**”)
- Consortiums grouping together Academic Laboratories / Commercial Applicants

The Applicants may comprise separate legal entities, and a key contact for CRYOSTEM should be clearly identified by each Applicant (hereafter “**Project Initiator**”).

For projects of equal scientific value, projects presented by research teams belonging to a French Academic Laboratory will be preferred.

The Academic Laboratories taking part in establishing the Collection are authorized to respond to this Call for Projects. In the case of a joint response between a Commercial Applicant and an Academic Laboratory taking part in establishing the Collection, CRYOSTEM will be authorized to ask the parties to set forth in writing the motivations behind their desire to work together.

The appraisal and selection criteria of the Projects put forward by the Applicants will be submitted to international experts, thereby guaranteeing complete independence in the final choice of the Projects accepted.

PART II – TIMESCALE FOR THE CALL FOR PROJECTS

II.1 – Schedule for the Call for Projects

The application files and General Terms are available on demand (emilie.robert@cryostem.org or claire.fontenille@cryostem.org) and can be downloaded from the CRYOSTEM website (www.cryostem.org).

Projects submission to CRYOSTEM could be done at any moment of the year. Application files are studied during the Scientific Committee session following the project submission. Four sessions of the Scientific Committee at least are organised during the year.

II.2 - Application submissions

Applications will be sent to the following postal address:

Association CRYOSTEM
Institut Paoli-Calmettes
232 boulevard Sainte Marguerite
13009 Marseille

Or by e-mail to the project managers CRYOSTEM (emilie.robert@cryostem.org or claire.fontenille@cryostem.org).

For further information, please contact the project managers by phone (+334 91 22 34 37) or by e-mail (given above).

CRYOSTEM undertakes to take all appropriate measures in order to ensure the strictest confidentiality regarding the applications submitted. Applicants are however advised to perform all necessary procedures and take appropriate measures to protect the information that they provide within their response to the Call for Projects. Applicants should notify any possible conflicting interests and provide a list of the experts that they wish to challenge. CRYOSTEM undertakes to take this request into consideration where possible in order to guarantee the greatest possible fairness in the selection process.

II.3 - Description of the selection stages

First stage: Short-listing of Projects

This first stage aims to select the Projects that meet with the specific purposes set forth in the application.

With reference to the application, the following shall not be **accepted**:

- Incomplete applications;

- Applications written in French;
- Applications not signed by the person authorized to represent the Applicant.

At the end of this first stage, an unlimited number of Projects will be shortlisted by the Scientific Committee and examined in full as part of the second stage.

Applicants will be informed in writing of the result of this short-listing. No financial aid will be allocated to the Applicant on the basis of this first stage alone.

Second stage: Final selection of Projects

The second stage of the Call for Projects is the final selection stage of the Projects that will be chosen.

Each project will be sent to three (3) international experts. The final selection will be validated by the Scientific Committee and notified by the Steering Committee. The results of the Call for Projects will be notified to each Applicant.

The final selection criteria may be communicated for information purposes and on request from an Applicant to CRYOSTEM.

No financial aid will be allocated to the Applicant at the end of this second stage.

II.4 – Selection of Projects

Appraisal of the applications submitted by the Applicants will take place on the basis of criteria defined by CRYOSTEM. These criteria may be provided for information purposes and on request from the Applicant to CRYOSTEM.

Some information from the selected projects (title, name of the principal investigator and related laboratory, synthesis, key words, Layman’s summary...) could be presented on the CRYOSTEM website (www.cryostem.org).

PART III – BRIEF PRESENTATION OF THE CONDITIONS OF USE OF THE SAMPLES MADE AVAILABLE TO THE CHOSEN APPLICANTS

III.1 – Conditions governing access to the samples

The Collection includes three types of samples: viable cells in DMSO, dried cell pellets and plasma.

The samples made available by CRYOSTEM in relation to a Project accepted as part of the Call for Projects will be selected by CRYOSTEM in accordance with relevance criteria in relation to the Project (hereafter the “**Samples**”).

The clinical data required for the Project to progress smoothly will be made available with the Samples.

CRYOSTEM reserves the right to select the Samples and restrict access to the Collection according to qualitative, quantitative and financial criteria.

The process for selecting the samples may be provided, for information purposes, to a selected Applicant upon submission to CRYOSTEM of a written request to this effect.

III.1.1 Availability of the Samples

CRYOSTEM will inform the Applicant of the planned date of availability of the Samples.

The delivery of the Samples will be organized by CRYOSTEM, which reserves the right to choose the means of transport. The carriage costs of the Samples will be borne by the Applicant and billed at their actual cost. The Applicant may receive information about the amount of the applicable carriage costs, upon submission of a request to CRYOSTEM.

Once the Samples are received, the Applicant is responsible for inspecting their condition and setting forth any reservation or protest regarding their physical state, within a period of eight (8) days as of the date of receipt of the Samples.

The Applicant commits to return to the project managers the provided samples follow-up sheet, after any use.

III.1.2 Right to use the Samples

The Samples may be used for research purposes, respecting individual rights and the legal and ethical principles governing the status of the human body, its parts and its products, without any right to transfer them.

CRYOSTEM and the SFGM-TC will provide clinical data of interest for the Project in relation to the Samples selected by CRYOSTEM.

III.1.3 Suspension – Return of the Samples

Any use of the Samples other than that defined and authorized by CRYOSTEM is strictly prohibited.

Failure by an Applicant to abide by the conditions of use defined by CRYOSTEM upon selecting the Applicant may lead to the suspension of availability of the Samples, and the return to CRYOSTEM of the Samples already provided, at the Applicant's cost.

III.1.4 Financial Conditions

The Samples made available to the Applicant will be accessible in accordance with the financial terms defined in Appendix 2.

These prices include the pre-analytical costs, the costs of selecting the Samples of interest, removal from storage, export of the related clinical data and the continued existence of the Collection.

The availability of the Samples is part of an operation that is not subject to value-added tax in accordance with the terms of article 256 of the French Tax Code and the Official Bulletin of the French Tax Authorities BOI-IS-CHAMP-10-50-10-20.

III.2 – Obligations

III.2.1 CRYOSTEM's Obligations

CRYOSTEM is bound by an obligation of means as regards making the Samples available to the Applicant. CRYOSTEM is also bound by an ISO 9001-2008 certification process including the surveillance of the BRC for the management of the Collection in accordance with the requirements of standard NF S 96-900. The Samples included in the Collection have therefore been prepared in accordance with a standardized procedure defined by CRYOSTEM. This procedure is applied by all members of CRYOSTEM in accordance with good laboratory methods.

CRYOSTEM regularly inspects that these methods are respected and performs random quality tests on the Collection at least once per year, the results of which may be provided to the chosen Applicant, upon submission to CRYOSTEM of a written request to this effect.

Some Samples, by their very nature, may not present all of the characteristics required, which is specifically acknowledged by the Applicant. The Applicant undertakes not to claim that CRYOSTEM replaces the Samples which do not meet its expectations.

CRYOSTEM guarantees, to the exclusion of any other guarantee, that the Samples have been prepared in accordance with the “standardized procedures regarding samples and data” drawn up by CRYOSTEM.

In particular, CRYOSTEM may not be held liable for any damage to the Samples in the Applicant's premises, or for their mishandling by the Applicant, as the latter bears exclusive responsibility for Sample storage.

III.2.2 Applicant's Obligations

The chosen Applicant undertakes to inform CRYOSTEM regularly concerning the progress of the Project, and to provide a progress report, at the latest eighteen (18) months after the selection of the Project by CRYOSTEM, along with a final report at the end of the Project. However, the chosen Applicant might be asked for intermediary reports on demand of the Scientific Committee or the potential sponsors or for communication actions. The chosen Applicant undertakes to inform CRYOSTEM of the end of the Project within three (3) months following the end of the Project.

The chosen Applicant undertakes to inform CRYOSTEM project managers of any relevant information related to the Samples quality in link with their use in a reasonable delay following the session.

The chosen Applicant undertakes to destroy the Samples within a period of thirty-six (36) months from the time when the research programme approved by CRYOSTEM is completed. A destruction certificate must be sent to CRYOSTEM upon expiry of this period.

However, the Applicant benefiting from CRYOSTEM's Samples may, within this period of thirty-six (36) months following the end of the Project, ask for authorization from CRYOSTEM to use the Samples for another research project.

This project must be submitted beforehand to CRYOSTEM Scientific Committee. The Scientific Committee undertakes to examine the said project involving the Samples already provided and to provide its decision within a period of two (2) months. CRYOSTEM will communicate the Scientific Committee decision to the Applicant which undertakes to abide by it.

The chosen Applicant is explicitly prohibited from performing research on the Samples provided by CRYOSTEM outside of the scope of the Project for which CRYOSTEM has given its approval. This ban includes all clinical data provided by CRYOSTEM and the SFGM-TC in relation to the Samples provided by CRYOSTEM as part of the project.

III.3 – Intellectual Property

The Applicants undertake to declare the intellectual property rights that they own in relation to the Project that they are submitting as part of the Call for Projects.

CRYOSTEM co-owns the results obtained with the Samples from the Collection.

The conditions governing the use of the results obtained with the Samples from the Collection are specified in articles III.3.1 and III.3.2 below.

III.3.1 Special terms for “Academic Laboratory” Applicants

“Academic Laboratory” Applicants are prohibited from making further direct use of the results from the research programme authorized by CRYOSTEM.

In the case of patentable or useable results, or results involved in a partnership between the “Academic Laboratory” Applicant and a Commercial Applicant, CRYOSTEM may grant a non-exclusive co-development right subject to joint use with CRYOSTEM.

The minimum financial conditions and the imperative obligations will be discussed mutually between CRYOSTEM and the “Academic Laboratory” Applicant, prior to the undertaking by the said Applicant of the initial negotiations, and will be set forth in a “development delegation letter” drawn up by CRYOSTEM in favour of the said Applicant.

The minimum conditions will be set forth lastly by CRYOSTEM. However, should a dispute arise, the “Academic Laboratory” Applicant may, at its cost, appoint a financial appraiser registered on the list of court experts.

The expert's assignment will include the encounter between CRYOSTEM and the “Academic Laboratory” Applicant in order to gather their respective arguments for setting the minimum financial conditions proposed by both parties, and the drafting of a report proposing a range of minimum values, and the grounds for the said range.

If the value proposed by CRYOSTEM is included in the said range, this value will be accepted.

If the value proposed by CRYOSTEM differs by more than 10% from the nearest outer limit of the range set forth by the expert, the value accepted will be that of the nearest outer limit.

If the value proposed by CRYOSTEM differs by more than 50% from the nearest outer limit of the range set forth by the expert, the value accepted will be that of the nearest outer limit and CRYOSTEM will also reimburse the appraisal costs up to a maximum amount of €5,000 excluding VAT per appraisal.

III.3.2. Special terms for “Commercial Applicants”

CRYOSTEM and the chosen “Commercial Applicant” will be co-owners of the results obtained with the Samples made available as part of this Call for Projects. The parties shall meet immediately and in any event prior to publication or disclosure of the results, in order to decide on the possibilities for patenting the said results.

If it is deemed appropriate to patent the results, the parties will file a patent application in both names, of which the ownership and each party’s rights and obligations will be governed by the terms of the standard co-ownership agreement available on request to the project manager.

For each new invention to be patented, CRYOSTEM and the applicant will sign a co-ownership agreement that complies with the standard agreement.

III.4 – Right to publication

The chosen Applicant undertakes to refer to CRYOSTEM and the SFGM-TC in any publication in relation to the Project in accordance with the following conditions:

- By quoting CRYOSTEM in the list of authors and by listing in the appendix the members of the Steering Committee, the Strategic and Scientific Committee and the Plenary Committee (complete list to be obtained from CRYOSTEM)
- By noting the origin of the Samples in the “Materials and Methods” section in the following format *“The samples annotated have been provided by the CRYOSTEM and SFGM-TC Consortium.”*

The Applicant undertakes to include CRYOSTEM logo, provided to him, in any oral and written communication.

Any quotation of CRYOSTEM biological Samples used by the chosen Applicant will follow the CoBRA guideline for the citation of biological resources.

The Applicant undertakes to submit the draft publication to the Scientific Committee at least one (1) month prior to publication, for its opinion, so that CRYOSTEM can check its accuracy.

CRYOSTEM will inform the Applicant of its decision within a maximum period of fifteen (15) days from when the project is sent. Should no response be received within this period, CRYOSTEM’s consent will be deemed to have been provided.

Consequently, CRYOSTEM may make any amendment or suspend the draft publication if any information due for publication presents omissions or inaccuracies.

PART IV – FINAL TERMS

IV.1 – Dispute settlement

The parties shall endeavour to settle their disputes on an out-of-court basis or via a mediator.

Otherwise, the parties will settle their dispute before the *Tribunal de Grande Instance* in Paris.

IV.2 – Applicable law

These General Terms are governed by French law. In the case of their translation into a foreign language, only the French text will be binding.

IV.3- Acceptance of the General Terms

The submission of an application by an Applicant implies the latter's specific and unreserved acceptance of all of these General Terms.

- Qualified members in Stem Cell Transplantations and / or Hematology:
 - Pr Gérard Socié, head of Hematology Units, Saint Louis hospital, Paris
 - Pr Mohamad Mohty, head of Clinical Hematology and Cell Therapy, Saint Antoine hospital, Paris
 - Pr Marie-Thérèse Rubio, PU-PH Clinical Hematology, head of the transplantation programm, Nancy
 - Pr Frédéric Baron, PU-PH Clinical Hematology, head of the transplantation programm, Liège

- The chairman of the SFGM-TC Scientific Committee or a representative

- Members of Steering Committee:
 - Pr Régis Peffault de Latour, project Coordinator, PU-PH Saint-Louis hospital, Paris
 - Pr Jean-Hugues Dalle, PU-PH Paediatric Hematology, Robert Debré hospital, Paris
 - Dr Boris Calmels, BRC Coordinator, PH in Cell Therapy Centre of « Institut Paoli-Calmettes » Marseille
 - Mrs. Claire Fontenille, Project manager
 - Mrs. Emilie Robert, Project manager

**Pricing list covering
the provision of samples from the CRYOSTEM Collection**

A : Academic project initiator and member of the CRYOSTEM consortium
B : Academic project initiator unaffiliated with the CRYOSTEM consortium
C : Non-academic / private / commercial project initiator

by aliquot*	A	B	C
mononuclear cells in DMSO	12.00 €	15.00 €	42.00 €
dry precipitate	9.00 €	11.25 €	31.50 €
plasma	8.00 €	10.00 €	28.00 €
nitrogen storage (per year) ¹	0.80 €	1.00 €	2.80 €
removal from storage (flat rate) ²	5.40 €	6.75 €	18.90 €
blood sample (flat rate)	8.80 €	11.13 €	30.80 €

by patient**	A	B	C
selection and unpacking of aliquots	15.00 €	18.75 €	52.50 €

by project	A	B	C
extraction of clinical data	280.00 €	350.00 €	700.00 €

by group from 1 to 200 aliquots**	A	B	C
shipment (flat rate) ³	225.00 €	225.00 €	225.00 €
centralisation ⁴ , control and shipment to the PI (flat rate)	46.00 €	57.50 €	161.00 €

* Single aliquot = 1 x 2ml cryotube

¹ To be multiplied by the storage duration for each aliquot set at 2 years

² Including extracting biological data

** Unlimited number of aliquots for a single patient

³ To be multiplied by the number of expeditions to the platform in Marseille and then onwards to the Project initiator

⁴ Shipment in dry ice from CRB partners to the CRYOSTEM platform, then onwards to the Project initiator