FREGAT RESOURCE ACCESS AGREEMENT

Constitution of a French nationwide clinical and biological database for oesophageal and gastric cancer

www.fregat-database.org

Approval	Name	Date	Signature
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Background

France is particularly affected by oesophageal and gastric cancer; the country notably has the highest incidence of oesophageal cancer in Europe. In 2011, 4,280 new cases of oesophageal cancer and 3,440 deaths were recorded, and there were 6,440 incident cases of gastric cancer and 4,430 deaths. The prognosis for these cancers is particularly poor, with an overall 5-year survival rate of 10-15% for patients with oesophageal cancer and 25% for patients with stomach cancer.

Whereas surgery is the benchmark treatment with curative intent, it does not result in prolonged recovery in most cases. Various combinations of surgery, endoscopy, chemotherapy, radiotherapy and targeted therapies are frequently required. Even though the survival rate is increasing, a large number of patients will present:

- advanced cancer at the time of diagnosis.
- a lack of response or poor response to treatment.
- early relapse.
- impaired quality of life.

Today's treatment approaches are general and rarely focus on particular subgroups of at-risk patients. Furthermore, there is less research on oesophageal and gastric cancer than on other cancers.

The creation of a nationwide, prospective cohort of patients with oesophageal and gastric cancers (including epidemiological, clinical, surgical, tumour-related, follow-up, and human and social science data, a tumour bank, and a blood bank) is thus major, critical issue in France. This research must involve a personalized approach, in order to identify the clinical, biochemical and oncological determinants of cancer treatment resistance and explain the epidemiological, social and behavioural characteristics.

The FREGAT database of clinical and biological data (developed as part of a biomedical research project sponsored by Lille University Hospital and funded by the French National Cancer Institute (INCa)) will thus constitute a large, ambitious programme for addressing these issues. FREGAT brings together a very high proportion of the clinical research groups at Lille University Hospital and the cancer centres that treat most of the region's patients with oesophageal and gastric cancer.

The present resource access agreement sets out the terms and conditions for accessing and using the resources generated by the FREGAT cohort.

1. Definitions

FREGAT database	The database containing all the data generated by the FREGAT Cohort.
Scientific Advisory Board	The Scientific Advisory Board in its plenary and core configurations.
Investigating Centre	Each clinical study site that includes and monitors Cohort Patients.
Access Agreement	The present document, notably defining access to the Cohort's Resources for the Study Sponsor, the Academic Partners, and the Industrial Partners.
Project Manager	The Sponsor's coordinating CRA in charge of oncology or any other person designated as Project Manager by the Study Sponsor.
Cohort	The biomedical research study entitled "Constitution of a French national clinical and biological database of oesophageal and gastric cancers" (FREGAT), sponsored by Lille University Hospital (French national study registration number (ID-RCB): 2013-A01281-44).
Collection	The collection (created for scientific purposes) constituted by the Patients' Biological Samples and any derivatives of the said Samples.
Scientific Coordinator	Professor Guillaume Piessen or any other representative designated by Lille University Hospital as the Scientific Coordinator.
Assistant Scientific Coordinator	Professor Antoine Adenis or any other representative designated by Lille University Hospital as the Assistant Scientific Coordinator.
Data	All of the FREGAT Database's data relative to or associated with the Cohort's Patients and the Biological Samples, including clinical and biological data.
Biological Samples	All the biological samples collected from the Patients, notably including blood samples and tumour biopsies.
Study Sponsor	Lille University Hospital, which initiated the FREGAT study and manages the Cohort and the Collection.
Industrial Partner	Any private-sector research group contributing to the Cohort and that may at some point submit its own Scientific Research Project (SRP), for validation and management under the terms and conditions set out in the present Access Agreement.
Academic Partner	Any public-sector research group that may at some point submit its own Scientific Research Project (SRP), for validation and management under the terms and conditions set out in the present Access Agreement.
Patient	The person suffering from cancer of the oesophagus and/or stomach and having been recruited by an Investigating Centre as part of the FREGAT Cohort.
SRP Leader	The person responsible for an SRP.
Proprietary Product	The healthcare product to which the Industrial Partner owns intellectual property rights or rights of use.
Scientific Research Project (SRP)	Any Scientific Research Project presented by a Partner and approved by the Scientific Advisory Board.
Resources	The Data, the FREGAT Database, the Collection, and the Biological Samples.
Results	Any technical and/or scientific information and knowledge (whether patented or not or patentable or not), including know-how, software (as source code or object code), plans, diagrams, drawing, equations or any other type of information in any form, and the associated rights obtained during the performance of an SRP.

2. List of abbreviations

CRA: clinical research associate

CRF: case report form

BRC: biological resource centre
DTA: data transfer agreement
FREGAT: “FRench EsoGastric Tumours”
INCa: [French] National Cancer Institute
MTA: material transfer agreement
SRP: scientific research project
CST: clinical study technician

3. Governance

The Cohort is under the governance of Lille University Hospital.

The FREGAT Cohort has the following governing bodies:

- the **Strategy Committee**
- the **Scientific Advisory Board**
- the **Steering Group**

3.1 The Strategy Committee

➢ Duties

The **Strategy Committee** has the following duties:

- To approve the Cohort’s scientific and strategy policies.
- To validate the annual report drafted by the Steering Group.
- To validate the FREGAT project’s budget proposed by the Steering Group.
- To validate the distribution of funding proposed by the Steering Group.
- To validate the rules concerning the management of relationships of interest and conflicts of interest.
- To define how the Cohort is evaluated prior to any decision concerning its possible termination or its renewal after the initial period.
- To validate the Access Agreement and (if required) modify it.
- To decide (after consulting the Steering Group) on the withdrawal of permission to access and use the Resources.
- To decide on the entry criteria for Industrial Partners.
- To define the composition, duties, and operating procedures for any Governing Body whose implementation is judged to be required for the Cohort.
- To appoint the members of the Core Scientific Advisory Board.
- To determine the policy on non-scientific public relations.
- To rule on any other question not explicitly dealt with by another Governing Body (notably the replacement of the Scientific Coordinator or the Assistant Scientific Coordinator).

➢ Composition

- The Scientific Coordinator (Chairperson)
- The Assistant Scientific Coordinator
- The Research Director of Lille University Hospital or his/her representative
- The Study Sponsor’s Medical Coordinator or his/her representative

Guest members

- The FREGAT Project Manager
- The study Sponsor's oncology coordinator
- One of the Study Sponsor's clinical research associates (CRAs)

When required and following a proposal by the Chairperson, the Strategy Committee can invite qualified persons to give advice or make recommendations on a topic on the Committee's agenda. The persons invited by the Strategy Committee shall only act in an advisory capacity during the meetings and shall sign a confidentiality agreement prior to the meetings.

The Strategy Committee's composition on the date of validation of the Access Agreement is given in Appendix 1.

➢ Operating procedures

The Strategy Committee is convened by the Chairperson or the Study Sponsor and meets at least once a year or as necessary. Decisions are taken by a majority vote.

3.2 The Scientific Advisory Board

3.2.1 The Plenary Scientific Advisory Board

3.2.1.1 Duties

The **Plenary Scientific Advisory Board**:

- Ensures the coherence and scientific quality of the Cohort through scientific management and coordination.
- Suggests scientific strategies to the Core Scientific Advisory Board.
- Reviews the SRPs validated by the Core Scientific Advisory Board and makes observations on the said projects.
- Presents feedback from the Investigating Centres.

3.2.1.2 Composition

- The Scientific Coordinator (Chairperson).
- The Assistant Scientific Coordinator.
- The Lead Investigators from each Investigating Centre.

The Plenary Scientific Advisory Board's composition on the date of signature of the Access Agreement is given in Appendix 2.

3.2.1.2 Operating procedures

The Plenary Scientific Advisory Board is convened by the Chairperson and shall meet at least once every twelve months or as necessary.

3.2.2 The Core Advisory Board

3.2.2.1 Duties

The **Core Scientific Advisory Board**:

- submits scientific and strategic advice on the Cohort to the Strategy Committee.
- gives non-binding advice on the Access Agreement.
- evaluates the relevance and scientific quality of the SRPs, selects the SRPs according to the terms of the Access Agreement, and prioritizes the SRPs.
- grants the leader of academic SRPs a period of exclusive use of the results generated by the SRPs. After this period of exclusive use, the data can be used by all the private- and public-sector research groups, according to the terms and conditions of the present agreement.
- suggests that the Steering Group removes permission to access and use the Resources granted to an SRP leader if the latter does not comply with the terms and conditions of the Access Agreement.
- validates the communications and publications generated by the SRPs.
- monitors the scientific quality of the SRPs and the publications generated by the SRPs.
- helps the Steering Group to draft the scientific part of the Cohort's annual report.

3.2.2.2 Composition

- The Scientific Coordinator (Chairperson)
- The Assistant Scientific Coordinator
- 5 members representing the surgeons
- 6 members representing the oncologists
- 2 members representing the pathologists
- 2 members representing the BRCs
- 2 methodologists.
- One representative from the human and social sciences.

Invited members:

- The FREGAT Project Manager
- The study Sponsor's oncology coordinator
- A legal expert
- One of the Study Sponsor's CRAs.

The members of the Core Scientific Advisory Board are nominated for a period of 3 years by the Strategy Committee, with the exception of the Scientific Coordinator and the Assistant Scientific Coordinator (permanent statutory members).

Each member of the Core Scientific Advisory Board can ask the Chairperson to nominate a deputy member to represent them when absent.

If a member resigns or repeatedly fails to attend meetings, the Core Scientific Advisory Board can ask the Strategy Committee to nominate a replacement.

The composition of the Core Scientific Advisory Board must be as representative as possible of the regions in which the majority of the patients have been included.

As necessary and if proposed by the Chairperson, the Core Scientific Advisory Board can ask qualified persons to give advice or make recommendations on an item on the agenda. The persons invited by the Core Scientific Advisory Board shall only act in an advisory capacity during the meetings and shall sign a confidentiality agreement prior to the meetings.

The Core Scientific Advisory Board's composition on the date of signature of the Access Agreement is given in Appendix 3.

3.2.2.3 Operating procedures

The Core Scientific Advisory Board is convened by the Chairperson and shall meet at least once every six months or as necessary.

Decisions shall be taken by a majority vote among the members present. If the votes are split equally, the Chairperson shall have a casting vote. The minutes of the Core Scientific Advisory Board's meetings shall be drafted by the FREGAT Project Manager (with the assistance of a CRA), validated by the Scientific Coordinator, and then e-mailed to the Core Scientific Advisory Board's members.

3.3 The Steering Group

3.3.1 Duties

The **Steering Group** has the following duties:

- To establish the Cohort's annual report (in collaboration with the Core Scientific Advisory Board for the scientific part).
- To ask the Strategy Committee to budget the distribution of funding obtained.
- To ensure the Cohort's implementation and operational follow-up; this notably involves monitoring the Cohort's staff (CRAs, CSTs, etc.), monitoring the inclusion rates at the Investigating Centres, identifying potential operational problems at the Investigating Centres and, as necessary, suggesting solutions.
- To elaborate the procedures required for operation of the Cohort and the Access Agreement (access to the data and Biological Samples, publication rules, etc.).
- To monitor compliance with deadlines (with regard to Industrial Partners, the INCa, etc.).
- To set the Scientific Advisory Boards' agendas.
- To suggest the nomination or renewal of the members of the Core Scientific Advisory Board to the Strategy Committee.
- To define the procedures for managing conflicts of interests.
- To make recommendations to the Core Scientific Advisory Board on the methodology and feasibility of SRPs.
- To give an opinion on any withdrawal of authorization of access to the Resources suggested by the Core Scientific Advisory Board.
- To monitor the operational aspects of SRPs with the scientific leaders.
- To coordinate access to the Samples and the Data as part of SRPs, after receiving the Core Scientific Advisory Board's opinion.
- To extend the non-scientific public relations validated by the Strategic Committee (website, communication with patients, press releases, etc.).

3.3.2 Composition

- The Scientific Coordinator (Chairperson)
- The Assistant Scientific Coordinator
- A person representing the BRCs
- A person representing the tumour banks
- A person from the human and social sciences
- The FREGAT project manager
- The study Sponsor's oncology coordinator
- A data manager
- A CRA

Each member of the Steering Group can ask the Chairperson to designate a deputy member authorized to participate in the member's absence.

As necessary and if proposed by the Chairperson, the Steering Group can ask qualified persons to give advice or make recommendations on an item on the agenda. The persons invited by the Steering Group shall only act in an advisory capacity during the meetings and shall sign a confidentiality agreement prior to the meetings.

The composition of the Steering Group on the date of signature of the Access Agreement is given in Appendix 4.

3.3.3 Operating procedures

The Steering Group meets (after being convened by its Chairperson) at least once every six months or as often as necessary.

Decisions shall be taken by a majority vote among the members present. If the votes are split equally, the Chairperson shall have a casting vote. The minutes of the Steering Group meetings shall be drafted by the FREGAT Project Manager (with the assistance of a CRA), validated by the Scientific Coordinator and then e-mailed to the members of the Steering Group and the Study Sponsor's representatives on the Strategy Committee.

4. Procedures for accessing the Cohort Resources

All research groups (whether from the public or private sectors and whether located in France or abroad) wishing to use the Resources in an SRP must submit the said SRP to the Core Scientific Advisory Board. It may concern use of the Data and/or the Biological Samples.

The SRP Leader associated with the Cohort is responsible for the quality and scientific integrity of the SRPs.

The SRP Leader is also responsible for providing the funding required to perform the SRPs. The Leader is responsible for the implementation and advancement of the SRP. The SRP Leader also undertakes to send an annual progress report on the SRP to the Core Scientific Advisory Board. He/she undertakes to send the full results of the SRP to the Study Sponsor no later than 2 months after the end of the said project.

4.1. Groups that lead an SRP

The Cohort Resources are potentially accessible by all research groups, whether from the public or private sectors and whether located in France or abroad.

Any application for use of the Resources shall be the subject of an SRP presented for validation to the Cohort's Core Scientific Advisory Board.

The research group leading the SRPs shall ensure that the Resources:

- are used for the sole purposes of performing the SRPs as set out in the project application validated by the Core Scientific Advisory Board.
- are not exported abroad without the specific written agreement of the Study Sponsor.
- are not distributed or transferred to a third party, except after the signature of an agreement between the Study Sponsor and the said third party.
- are stored and used only in compliance with the laws and regulations applicable to the Resources concerned, and are stored and used exclusively on its premises by scientists and research groups working under its direct responsibility.

If Biological Samples are transferred, the group leading the SRPs undertakes to track the said samples and to guarantee compliance with the rules on hygiene, safety, environmental protection, and labour.

4.2.Cohort Resources concerned by the applications

Data or Biological Samples shall only be transferred within an SRP that has a detailed analysis plan with a precise scientific objective and a clearly established purpose. The SRP must notably mention the list of the variables required for performance of the said project, which that will be reviewed and validated by the Core Scientific Advisory Board.

4.2.1. Cohort Data

Access to the following Cohort Data may be requested:

Aggregate data

The aggregate data are constituted from the FREGAT Database and result from the combination of the CRF's different variables. They are obtained by statistical processing of the individual Data (mean value, percentage, sum etc.). They provide information on groups of Patients who share characteristics. These Data are aggregated by the Study Sponsor under the supervision of the Scientific Coordinator.

Non-anonymised raw Data

No non-anonymised raw Data from the FREGAT Database shall be transferred, except with the prior, written agreement of the Study Sponsor and the competent authorities.

Pseudoanonymised raw Data

For Academic Partners, access to pseudoanonymised raw Data will be granted by the Core Scientific Advisory Board on a case-by-case basis, subject to approval by the Steering Group.

It should be noted that Industrial Partners cannot access the raw Data and can only access aggregate data and/or data derived from the raw Data.

The price of supplying, transferring and/or potentially analyzing these Data will be set in a quote established by the Study Sponsor in compliance with the FREGAT pricing table, and will be subject to a jointly agreed contract between the organisation to which the research group leading the SRP is attached and the Study Sponsor.

4.2.2. The Cohort's Biological Samples

Access to the Biological Samples is only possible as part of an SRP that has been reviewed and validated by the Core Scientific Advisory Board; the latter gives a reasoned opinion on each SRP, according to the evaluation grid presented in Appendix 5, and which notably covers:

- the SRP's relevance and scientific validity.
- the scientific objectives of the Cohort Partners' research groups.
- the priority given to access to the Biological Samples by the Cohort Partners' research groups.
- the priority given to multicentre research projects.
- the quantity of Biological Samples required for performance of the SRPs.

Given the consumable nature of the Biological Samples and thus the need to optimise the use of the Resources, the Core Scientific Advisory Board has the right to veto SRPs presented to it.

Furthermore, the Chairperson of the Core Scientific Advisory Board has the right to veto SRPs that clash with the Cohort's scientific objectives or with another SRP previously validated by the Core Scientific Advisory Board.

The remaining Biological Samples will be sent back to the BRC from which they were obtained, unless otherwise approved by the Core Scientific Advisory Board and the Study Sponsor.

The Investigating Centres shall have high-priority access to the Biological Samples, which will be determined by the Core Scientific Advisory Board notably as a function of their involvement in the Cohort's operation.

The price of supplying, transferring and/or potentially analyzing the Biological Samples will be defined in a quote established by the Study Sponsor in compliance with the FREGAT pricing table, and will be subject to a jointly agreed contract between the organisation to which the research group leading the SRP is attached and the Study Sponsor. It is understood that all transfers of Biological Samples shall be subject to a jointly agreed agreement (such as an MTA) between the organisation to which the research group leading the SRP is attached and the Study Sponsor.

4.3.Procedures for accessing the Resources

The Cohort's Resources can be accessed according to the following procedures.

4.3.1. Via the annual data dashboards

The Study Sponsor allows limited access to a selection of essential variables from the FREGAT Database via one of the data dashboards that are sent annually to all the Industrials Partners and Investigating Centres.

These data dashboards are visualization tools that present the current state of the Cohort, Data and Biological Samples collected and the profiles of Patients included at a specific time point. They are built with aggregate information from a selection of variables that are representative of the Patient profile at a given time point and/or over a defined period.

The data dashboards are tools that facilitate communication between the various public- and private-sector partners. They are considered to be confidential. No personal or professional reuse of the data dashboards (notably as oral communications at conferences or symposia) is authorized in the absence of prior written approval by the Cohort's Strategy Committee.

4.3.2. Via a feasibility study

The Academic and Industrial Partners can perform a preliminary feasibility study of an SRP in order to evaluate the power of the Cohort with regard to the requested SRP.

This feasibility study allows access to a limited number of aggregate data that are specifically selected with regard to the planned project.

The application for a feasibility study (which must cite all the Data required to evaluate the feasibility of the planned SRP)) shall be reviewed by the Core Scientific Advisory Board for validation and shall be subject to a jointly agreed agreement between the organisation to which the research group leading the SRP is attached and the Study Sponsor.

The results of the feasibility studies are considered to be confidential information. Their use other than for evaluating the feasibility of an SRP is not authorized.

4.3.3. Via Scientific Research Projects (SRPs)

4.3.3.1. Application for an SRP

Any public- or private-sector SRP Leader wishing to gain access to the Cohort's Resources is invited to fill out the application form given in Appendix 5, which will notably include the following information:

- administrative information, including the name of the SRP Leader and his/her organisation(s) and research group(s).
- the name of the industrial partner(s) potentially involved in the project and their role(s) and contributions to the project.
- the scientific questions and the project's methodological aspects.
- the list of the Data required for performance of the project.
- the type and the number of Biological Samples potentially required for performance of the project by precisely justifying the requested quantities of each type of Biological Sample.
- information attesting to the scientific excellence of the SRP Leader and of his/her research group (publications, collaborations, etc.).
- potential implications and specific requests concerning confidentiality.
- the SRP's provisional time line.
- the SRP's provisional budget.
- the source(s) of the project's public- or private-sector funding, specifying the nature and amount of each.
- A commitment to comply with the CNIL reference methodology to which the project relates.

The application forms are to be sent to the Core Scientific Advisory Board according to the terms and conditions set out in Appendix 5.

4.3.3.2. Review and selection of the SRPs

The SRP application form will be examined by the Core Scientific Advisory Board, which will review the file in detail.

The procedures for reviewing and selecting an SRP include the following steps:

4.3.3.2.1. Technical review of the SRP

The goal is to evaluate the application's admissibility, feasibility, and coherence:

- by checking that all items requested have been provided in the application form.
- by evaluating the admissibility of the project (feasibility, the match between the objectives and the suggested methodology, funding, etc.).
- by checking that the project is not redundant or in competition with one or more ongoing or planned scientific projects.
- by ensuring that the SRP's objectives do not conflict with those of the Cohort.

4.3.3.2.2. Scientific review of the SRP

The scientific review of the SRP is based on the following evaluation criteria:

- the relevance of the research on oesophageal and gastric cancers.
- the priority given to multicentre SRPs.
- the deliverables, relative to the state of the art.
- the relevance of the hypotheses and objectives, and their coherence with the Cohort's general objectives in the long term.
- the potential importance of the expected results.
- the project's innovative nature.

- the research perspectives.
- the results' academic value.
- the match between the project's methodology and objectives.
- the groups' comparability (for a comparative study).
- the match between the target population and the Cohort's patients.
- the presence or absence of bias.
- the project's structure and logic.
- the project's novelty and feasibility.
- the scientific quality of the applicant group (scientific environment, publications, and collaborations).
- the ethical, regulatory and public health aspects.

The SRP's scientific validity will be examined by at least 2 members of the Core Scientific Advisory Board, according to the evaluation grid given in Appendix 5. The Core Scientific Advisory Board shall call on third-party experts if specific expertise is required, subject to compliance with the rules on confidentiality.

After discussion, a reasoned decision is taken during a Core Scientific Advisory Board meeting.

4.3.3.3. Communication of the decision to the SRP Leader

The approval or non-approval decided by the Core Scientific Advisory Board and a summary of the comments will be communicated to the SRP Leader via the transmission of a full, anonymous report. The Core Scientific Advisory Board will make its best efforts to inform the SRP Leader of its decision within a month of the Core Scientific Advisory Board's meeting.

4.3.3.4. Financial conditions

The Academic Partners and the Industrial Partners may perform a feasibility study for an SRP, in return for a flat fee.

The costs related to activities required for the implementation of the SRPs (statistical analyses, etc.) will be covered by the research group leading the SRP.

The financial aspects of access to the resources will be set out in a quote issued by the Study Sponsor and in a jointly agreed contract between the organisation to which the research group leading the SRP is attached and the Study Sponsor.

4.3.3.5. Regulatory procedures

Each SRP Leader is responsible for identifying and implementing the regulatory procedures required for performance of the SRP. This includes, but is not limited to, all data protection compliance procedures, including establishing that the project complies with the applicable CNIL reference methodologies.

4.3.3.6. Final approval

When an SRP is approved, the specific procedures for collaboration between the Study Sponsor and the SRP Leader are formalized by the signature of a jointly agreed contract between the organisation to which the research group leading the SRP is attached and the Study Sponsor. The said contract formalizes the collaboration and any procedures for accessing and/or transferring the Data and/or Biological Samples derived from the Cohort.

This document shall notably specify the following points:

- the list of the Data to be transmitted.
- if applicable, the definition of the Biological Samples concerned.
- the periodicity and types of transfer (the recipient's name and contact details).
- Data protection procedures.
- confidentiality clauses.
- if applicable, clauses on exclusive use.
- the project monitoring procedures, including the option for terminating the SRP before it has finished by decision of the project leader or the Strategy Committee, and the obligation to send the Study Sponsor the full results of the project no later than 2 months after the end of the said project.
- procedures for publishing the Results.
- publication rules.
- financial clauses.
- appendices: copies of regulatory approvals and authorisations.

4.3.3.7. Provision of the Data

Any transfer of Data must have a defined, explicit, legitimate purpose described in a study protocol that shall specify the type of variables transferred, the transfer procedures, the data storage procedures in the recipient group, the duration of use, and the data ownership rules.

The transferred Data must not subsequently be processed in a way that is incompatible with the said purpose. The Data must be sufficient, relevant and non-excessive with the regard to the said purpose and be strictly anonymous. The SRP Leader shall ensure that any use of raw data as part of an SRP is performed exclusively by people qualified in the field of biostatistics and clinical research methods.

The analyses must only cover what has been stated in the SRP application form validated by the Core Scientific Advisory Board. Consequently, only the Data set out in the form can be requested from the Study Sponsor.

If the initial SRP changes (with regard to endpoints and objectives, etc.), a new SRP application form must be submitted.

As soon as the contract for the SRP between the SRP Leader's organisation and the Study Sponsor has been signed, the Study Sponsor shall prepare (in collaboration with the SRP Leader), the selected Data and will supply them by the most appropriate means and according to the jointly agree time line.

Data supplied by the Study Sponsor must not be transmitted to persons other than those scheduled in the SRP application. At the end of the study, the applicant will prohibit any subsequent use of the Data received from the Study Sponsor.

Supply of Cohort Data to foreign public-sector research groups:

Article 68 of France's 1978 Data Protection Act, the government decree dated October 20th, 2005, and the European General Data Protection Regulation (2016/679) prohibit the transfer of data outside the European Union, except when the recipient country or enterprise provides a sufficient level of protection for the transferred data (see the list on the CNIL website: www.cnil.fr).

Any transfer of data outside France requires prior approval of a data transfer agreement (DTA) that must be sent to the Study Sponsor before the SRP starts. In the event of data transfers to countries outside the European Economic Area (EEA), such as the United States, which, according to the EU, do not currently offer

an adequate level of protection for Personal Information, data controllers undertake to apply the European Commission's standard contractual clauses, supplemented by additional privacy protection measures enabling Personal Information to be protected in a manner at least equivalent to that required in the EEA.

4.3.3.8. Terms and conditions of Data use

The SRP Leader undertakes to use the Resources under the conditions set out in the SRP file validated by the Core Scientific Advisory Board.

It is up to each SRP Leader to ensure the technical security and confidentiality of Data used as part of his/her SRPs.

If the SRP changes (with regard to endpoints and objectives, etc.), a new SRP application form must be submitted and validated by the Core Scientific Advisory Board.

4.3.3.9. Monitoring of SRPs

Annual SRP progress reports are sent to the Core Scientific Advisory Board by the SRP Leaders. At the end of the SRP, the SRP's results are presented to the Core Scientific Advisory Board for final validation.

Furthermore, longitudinal SRPs are re-evaluated annually by the Core Scientific Advisory Board.

5. Intellectual property rules

5.1. The FREGAT Database

The FREGAT Database is owned by Lille University Hospital in its capacity as Study Sponsor.

5.2. Results of Scientific Research Projects (SRPs)

5.2.1. Academic SRPs

As part of an SRP submitted by an Academic Partner, the Results are the property of the Academic Partner.

In the case of a collaboration between several Academic Partners, the Results of the SRPs jointly owned by the participating Academic Partners, in accordance with the procedures defined in a jointly agreed contract between them signed before the start of the SRP.

5.2.2. Industrial SRPs

As part of an SRP submitted by an Industrial Partner:

- The Results not related to a Proprietary Product are jointly and equally owned by the Industrial Partner on one hand and by the Study Sponsor on the other.
- For Results related to a Proprietary Product, the Industrial Partner (the owner of the product concerned) has the right to exclusively exploit the Results related to its Proprietary Product, in accordance with financial conditions defined in a joint agreement with the Study Sponsor.

5.3. Use and exploitation of the Results of an SRP

5.3.1. Rights to use the Results for research purposes

The Study Sponsor and the research group leading the SRP can freely and at no charge use the Results of the SRPs for in-house and collaborative research purposes, subject to the periods of exclusivity granted by the Core Scientific Advisory Board.

The data produced in the SRPs can be made available to the scientific community under the conditions set out in sections 4.2.1 and 4.2.2.

5.3.2. Rights to exploit the results for commercial purposes

Results not related to a Proprietary Product

As soon as one or more of the Academic Partners who own Results not related to a Proprietary Product consider the possibility of licensing the said results for commercial exploitation, the owner(s) must offer a licence to interested Industrial Partners. The licensing conditions will be specified in a jointly negotiated Result exploitation agreed prior to any exploitation of the Results.

Results related to a Proprietary Product

The Industrial Partner who owns the product has the right to exclusive exploitation of the Results related to its Proprietary Product.

The modalities of this exploitation are defined in a jointly agreed contract between the Industrial Partners involved and the Academic Partner(s) who jointly own the said results, as part of an exploitation agreement.

6. Publications/Communications

6.1.Public relations activities related to the Cohort

Publications or public relations activity related to the Cohort and intended for media serving the general public (regardless of the medium, including notably press releases, seminars, flyers, posters, videos and a website) are managed by the Study Sponsor.

This public relations activity may notably cover:

- the signature of collaboration agreements (with academic groups and/or industrial partners).
- the funding obtained from the INCa.
- the name of the Cohort and its general objectives (the Cohort's design and methodologies) in the terms defined by the Study Sponsor.
- summaries for the general public provided by the Study Sponsor.

6.2.Scientific publication or communication of the results

6.2.1. Authorship rules

The international rules on publications and authorship apply to all publications or scientific communications featuring the Cohort's Resources.

6.2.2. Summary of the international rules

An "author" is generally considered to be a person having made a significant scientific contribution to a published study. The title "author" will be reserved for people meeting all three of the following conditions:

- a substantial contribution to the conception of the Cohort or to analysis and interpretation of the Data.
- significant participation in drafting the article or revising it critically for important scientific content
- approval of the version to be published.

Acquisition of funding, collection of data or general supervision of a research group do not qualify a person for authorship. People having contributed to the project but whose contributions do not justify authorship

will be considered as non-author contributors. All people designated as authors must meet the criteria given above, and all people meeting these conditions should be identified as authors. Each author must have participated in the work sufficiently to be accountable for a part of the published Results.

6.2.3. FREGAT as an author: the FREGAT Working Group

For any publication based wholly or partly on the Cohort Data and/or SRP data, the words "*and the FREGAT Working Group"* must be included in the list of authors. This will enable a long list of contributors to the Cohort to serve as authors on the publication. All the names listed under the acronym *FREGAT Working Group* will therefore be considered as full authors and their names will be indexed by the National Library of Medicine.

The list of the names in the "*FREGAT Working Group***"** will vary and must be updated regularly.

This composition will reflect the different participants in the field of digestive oncology involved in the Cohort. Changes in the list of names must be logged. The composition of the "*FREGAT Working Group*" must be validated by the Core Scientific Advisory Board before the submission of each article.

6.3.Types of publication

For journal publications, it is necessary to specify [in French] that the "Centre Hospitalier Universitaire de Lille (CHU de Lille) est le promoteur de l'étude FREGAT" and (in English) "The FREGAT Study was sponsored by the Lille University Hospital".

Two types of publications have been defined:

6.3.1. Primary publications or communications

These are limited to primary (originator) publications or essential descriptive results meeting to the Cohort's main objectives. The list of these publications and communications is validated by the Core Scientific Advisory Board.

6.3.2. Publications or communication of SRP Results

These correspond to the publications resulting from an SRP, the analysis of which involves specific themes not covered by the primary papiers (i.e. the majority of the publications).

These must not hinder the publication of FREGAT's general results. The publications are subject to the same notification rules as the other types of publication. Each type of publication is governed by a precise set of authorship rules, as defined in the following table.

Type of publication	Authors	Nature of the publication
Primary publications	G. Piessen, A. Adenis, F Renaud and the FREGAT Working Group	Publications limited to the primary results or essential descriptive results
Publications of SRP Results	Individual authors (according to the international rules), G Piessen and 2 to 4 PI who included patient for this SRP and the FREGAT Working Group	Publications related to the ancillary projects that use the Cohort's Resources

6.4.Author contributions and operating rules

To guarantee efficiency and transparency during the review and approval of Cohort manuscripts and their submission to French or international journals, the authors must comply with the following procedure:

6.4.1. First draft and successive working versions

- The first author or the corresponding author circulates the draft to the co-authors.
- All the co-authors (including those listed under the name "*FREGAT Working Group"*) are encouraged to read and comment on the draft before the deadline set by the first author or the corresponding author.
- The main authors revise the draft with regard to the comments made by the co-authors.

6.4.2. Final version

- The final version must be circulated to the co-authors (including those listed under the name *FREGAT Working Group*) for approval. Failure to reply within the period of time defined by the corresponding author shall entail the withdrawal of the co-author's name from the list of authors.
- Before submission, the final versions of all papiers must be sent to the Core Scientific Advisory Board. The latter may make comments, particularly on the citation of FREGAT and the wording of acknowledgements.
- The final version of a primary publication resulting from an SRP must be approved by the Core Scientific Advisory Board.

6.4.3. Submission and revision process

- The corresponding author submits the publication and circulates this information to the co-authors (including those listed under the name "*FREGAT Working Group"*) by sending them the submitted version.
- All the authors will sign the copyright transfer agreement, conflict of interest form, authorship declaration and any other document requested by the journal. Failure to reply within the period of time defined by the corresponding author shall entail the withdrawal of the co-author's name from the list of authors.
- Depending on the editor's reply, the main authors will be responsible for revising the publication and re-submitting it to the same journal or another journal. The co-authors (including those listed under the name "*FREGAT Working Group"*) will be kept informed of the revision process by the corresponding author.
- The published version must be sent to the Scientific Advisory Board.

Each contributor (co-author) is responsible for informing the corresponding author and the Core Scientific Advisory Board of any change in his/her contact details. If a co-author cannot be contacted at any stage in the publication process, he/she will be excluded from the list of authors of the publication in question.

The full list of the "*FREGAT Working Group"* authors (names and contact details) will be provided on request, so that all the authors can be included in the papers' elaboration and revision process.

6.5.The "Acknowledgements" section

The Database's operators will be acknowledged as follows:
"We thank the Data Processing Centre for administration of the FREGAT Database and the provision of data."
"We thank the biological resource centres and tumour banks participating in the FREGAT project".

The acknowledgment for the Cohort's funding must be written as *"FREGAT is funded by the French National Cancer Institute (INCa)".*
The list of funding bodies is available on the website.

Depending on the paper, other funding bodies can be added: the PHRC [the French national funding programme for hospital-based clinical research] (PHRC reference, hospital, and year), etc.

6.6.The standard reference to be cited for the Cohort

Any publication relating to an SRP associated with the Cohort must cite at least one of the publications on the Cohort's methodology.

At present, the reference to be cited is "Mariette C, Renaud F, Piessen G, Gele P, Copin MC, Leteurtre E, Delaeter C, Dib M, Clisant S, Harter V, Bonnetain F, Duhamel A, Christophe V, Adenis A; Fregat Working Group. The FREGAT biobank: a clinico-biological database dedicated to esophageal and gastric cancers. BMC Cancer. 2018 Feb 6;18(1):139. doi: 10.1186/s12885-018-3991-8. PMID: 29409462; PMCID: PMC5801889".

6.7.The Cohort website **(https://www.fregat-database.org)**

Information about the project leaders may be released on the Cohort website. This will be information on the SRPs (title, description, keywords, publications, etc.) and also the name and the postal address of each participant in the SRPs. According to the French legislation on data protection, the project leaders have the right to access, modify, correct and delete their personal data. Given the characteristics of the Internet (i.e. the unrestricted capture of published information and the difficulty or impossibility of controlling third-party use of the said information), the project leaders can refuse to disclose their personal data (names, telephone numbers, etc.).

6.8.Appendices

Appendix 1: Composition of the Strategy Committee

Appendix 2: Composition of the Scientific Advisory Board

Appendix 3: Composition of the Core Scientific Advisory Board

Appendix 4: Composition of the Steering Group

Appendix 5: The SRP application form and project evaluation grid

Appendix 1: Composition of the Strategy Committee

- The Scientific Coordinator (Chairperson)
- Assistant Scientific Coordinators
- The Director of Research at Lille University Hospital or his/her representative
- The Study Sponsor's Medical Coordinator

Guest members

- The FREGAT Project Manager
- The study Sponsor's oncology coordinator
- One of the Study Sponsor's CRAs

Appendix 2: Composition of the Plenary Scientific Advisory Board

- The Scientific Coordinator (Chairperson)
- Assistant Scientific Coordinators
- The Lead Investigators from all the Investigating Centres

Appendix 3: Composition of the Core Scientific Advisory Board

- The Scientific Coordinator (Chairperson)
- Assistant Scientific Coordinators
- 5 members representing the surgeons
- 6 members representing the oncologists
- 2 members representing the pathologists
- 2 members representing the BRCs
- 2 methodologists.
- One representative from the human and social sciences.

Guest members

- The FREGAT Project Manager
- The Study Sponsor's oncology coordinator
- A legal expert
- One of the Study Sponsor's CRAs

Appendix 4: Composition of the Steering Group

- The Scientific Coordinator (Chairperson)
- Assistant Scientific Coordinators
- A person representing the BRCs
- A person representing the tumour banks
- A person from the human and social sciences
- The FREGAT Project Manager
- The study Sponsor's oncology coordinator
- A data manager
- A CRA

Appendix 5: The SRP application form and project evaluation grid