Quality of Life and Management of Living Resources

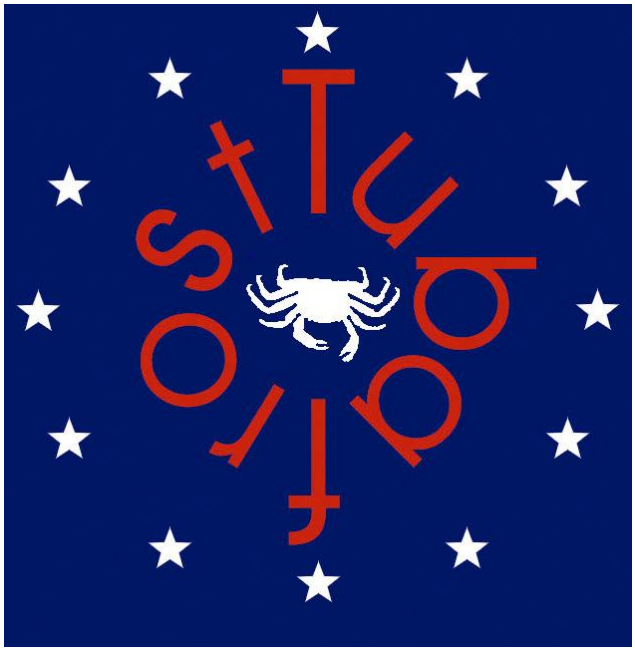
European Human Frozen Tumor Tissue Bank

TUBAFROST

QLRI-CT-2002-01551

Milestone MS 6.1

Report policy and rules for contribution to and use of banked tumor tissue in research



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Introduction

Since the 1980s, cancer research has largely shifted from using cell lines and animals to using tumor specimens. This has especially been the case for research focused on human tumors, for which there are relatively few good animal models [1]. However, in recent years, there is a rapidly growing realization that to fully exploit the genomic revolution in medicine will require the application of evolving molecular technologies to clinical tissue specimens [2]. The concept of 'molecular signatures', whereby the neoplastic tissue might be 'typed' according to the pattern of gene and protein expression, and correlated with cancer stage, prognosis and natural history [3-5], is an important step towards individualizing subsequent treatment selection, such as adjuvant chemotherapy, radiotherapy or treatment with mechanistically novel anticancer agents [6]. There is much current activity aimed at assessing a range of molecular markers that might allow definition of this poor prognostic subgroup and whether additional pharmacodynamic markers might select those individuals most likely to respond to particular cytotoxic drugs [7].

At this framework, the diagnostic and research purpose utilizing normal or tumor human tissues, the quality and integrity of study targets, such as genomic DNA, mRNA, and proteins is demanded [8]. In this regard, it has been estimated that by the year 2005, as much as 10% of clinical laboratory tests will be based on RNA or DNA analysis [9]. Moreover, specimens representing different stages of cancer development are required with an ever-higher quality and specificity. Take into account the special resource of a human, especially in a state of illness, a continuous, persistent guideline with specialized protocols for procurement, preservation, registration, and distribution of human tissues has been emphasized [10]. This means that significant efforts should be dedicated to obtain, not only high quality tissues , but also data on clinical outcomes which permits investigators to know that such data are available for analysis as they pursue their molecular studies on bank-derived specimens [11]. However, these efforts will be only be successful with the logical application of tumor banking and its associated informatics systems as the translational bridge linking new molecular information to its clinical significance [12-14].

Tissue banks and bio-repositories exist in almost every sector of scientific and medical communities and constitute a major source of human tissue constituting a tool for fundamental and translational research. But standards for collecting and storing tissue vary, and physicians sometimes have trouble gaining access to samples from centers other than their own. In this sense, one of the objectives of the TuBaFrost project is to stimulate cooperative efforts to collect and distribute human left-over fresh frozen tissues and to thereby facilitate research utilizing those specimens [15]. In addition, another purpose of Networking Tissue banks is to generate large quantities of tissue samples, giving rise to new effective critical masses to perform a new generation of experiments. These activities are expected to promote basic, developmental, and translational studies in many areas of cancer research including molecular biology, immunology, and genetics. Hence, integration of these bio-repositories in the TuBaFrost network, the first network of fresh frozen tumor tissues in Europe, will require the assessment of, not only a clear framework for report policy and rules for contribution to and use of banked tumor tissue in research, which, in the last term, is the scope of this milestone, but also the establishment of a legal Conduct Code according to the

legislation of the involved countries, as well as other tools (Virtual Tumor Bank, Quality control programs, standardized protocols for collecting and storing samples, etc.) that guarantee the excellence of the TuBaFrost strategy. This was only possible through a strong dialogue between the disciplines of the different Work packages of the TuBaFrost project and between the different Nationalities
The establishment of the incentives for collecting frozen tissue samples, access rules and use of the tissues has therefore been performed in close dialogue with the participating institutes during 4 TuBaFrost half yearly meetings, through 2 questionnaires, many emails, etc. to ensure smooth operation of the European Human Frozen Tumor Tissue Bank Network.

In order to define these report policy and rules for contribution to and use of banked tumor tissue in research, the TuBaFrost consortium developed the following tasks:

- ✓ Develop incentives for the participating institutions and their contributing pathologists.

- ✓ Define the rights and responsibilities of all participants concerning the use of the European Human Frozen Tumor Tissue Bank Network.

- ✓ Establish which rules are necessary for better use and control of banked tissues for research purposes:
    - o To set rules concerning quality control, validation of histo-pathological diagnosis, and protocols for representative digitisation and minimal data sets to accompany the samples.
    - o Develop a review system for proposed research, is replaced by the development of a more elaborate tissue request form.

In this last point, The TuBaFrost Consortium has decided that instead of developing a review system, an alternative method must be developed to get sufficient information on the requestor in an efficient way with the aim that the final decision as to the destination of the stored tissue will remain with the collector institutions. Therefore, an extended Tissue Request Form will be introduced, for which rules were established in deliverable 6.2.

According to these tasks, the following **policy report** has been established by the TuBaFrost consortium:

Chapter 1:
Preliminary considerations

1. Participation in the European Human Frozen Tumor Tissue Bank Network will be only possible for those European institutions, which can contribute tissues (collectors). These institutions must, in addition, be able to meet the demands set by the TuBaFrost consortium on minimum standards, protocols and quality control.

2. Access as a user or requestor to the European Human Frozen Tumor Tissue Bank Network will only be possible if the following conditions are met (all these conditions will be included the Tissue Request Form –see chapter 6 of this report

policy- and will help to collectors in making a choice regarding their stored samples):

- Requestor must be involved as a researcher in medical projects at any tumor research group.
- Requestor must be familiar with the European Code Proper Secondary Use of Human Tissue, which will be developed in WP 7.
- Requestor must be able to give an exact description of all planned research involving the tissue samples.
- Requestor must have permission of the local Medical Ethics Commission to execute the planned research.
- The planned research needs to be of sufficient quality to spend the valuable tissue samples on, to be judged by the individual collectors, which are involved in the application.
- Requestor must have sufficient expertise at its disposal to perform the planned research.
- Access should also be limited to those who are prepared to make a reference to the European Human Frozen Tumor Tissue Bank and the involved collectors of the tissue in future publications based on the results obtained on the received tissues (see also point 30).

3. In order to participate in the European Human Frozen Tumor Tissue Bank Network collectors will have to comply with criteria described in Annex I in order to guarantee the network strategy.

Chapter 2:
Incentives for participating institutions

4. The available samples in the European Human Frozen Tumor Tissue Bank Network will stay at the collector institutes. As a consequence the authority and responsibility for the tissue falls under the authority of the collector.

5. Participant institutions will not be forced to issue their tissue to projects they do not feel worthwhile. Hence, the final decision as to the destination of the stored tissue will remain with the collector institutes.

6. The collectors approached by the requestors make up the Tubafrost Tissue Transfer Agreement on their own authority (Annex II).

7. Collector institutes participating in the European Human Frozen Tumor Tissue Bank Network will open up their scientific perspectives, i.e.: participating in large-scale studies; accessing to larger homogeneous series of common and uncommon types of tumors; establishing multi-center connections; accessing to cost-intensive technologies; participating in an ethical, legal, standardized and quality framework.

Chapter 3:
Incentives for Pathologists/Scientists to contribute tissue

8. Pathologists will take a leading role in the creation of tumor banks for research in the collector institutions. In this way, pathologists will be involved in the field of research of the samples they have diagnosed.

9. Although all Pathologists in a collector institution can participate in the creation of a tumor bank, the collector institutes will name a member of the institute responsible in the elaboration of the specific tasks of the European Human Frozen Tumor Tissue Bank Network.

10. Financial rules in the forthcoming business plan will result in additional incentives for the contributing institutions. (For instance a reduction in cost recovery price by significantly lowering the consortium contribution part and reduction in the annual membership contribution for access, which can be earned back by offering well documented and wanted samples).

11. Participation in the creation of tumor banks will result in a number of incentives for the participating Scientist/Pathologists that could improve their professional career (opportunities to set-up co-operation between the requestor and tissue-issuing institute; access to rare tumor entities and large collections; rapid feedback on histology review –Virtual Microscope, in development by WP5-; feedback on results of research; co-authorship in the case of substantial contribution; preferred access through for instance financial discount for collectors to the TuBaFrost tissue collection; access to new biotechnology; etc.).

Chapter 4:
Responsibilities of all participants concerning the use of the European Human Frozen Tumor Tissue Bank Network

Chapter 4.1: *As a consortium*

12. The TuBaFrost consortium will set up a Steering Committee (or Steering Commission) once the TuBaFrost project has finished. The steering committee will serve as the governing board of the European Human Frozen Tumor Tissue Bank Network and will continue the activities of the consortium as a yet to be determined legal entity.

13. The TuBaFrost consortium members will constitute the Steering Committee from the team leader, or from a by the team leader indicated volunteering person per TuBaFrost consortium member for this position.

14. One chairperson will be selected by the Steering Committee who will have coordinating functions. He/She will be responsible for coordinating the activities of the Steering Committee, for preparing meeting agendas and for scheduling and chairing meetings. The chairperson will prepare annual progress reports, which will include individual reports from each member of the European Human Frozen

Tumor Tissue Bank Network. The steering committee will decide after what time period re-election of the chairman takes place.

15. The Steering Committee will have primary responsibility for promoting the European Human Frozen Tumor Tissue Bank Network and for assuring the distribution of highly quality tumor samples for cancer research projects. This Committee will also promote and perform research activities related to tumor banking.

16. To protect the quality of the samples entered in the central database the Steering Committee will judge applications from tissue collecting institutes to join the TuBaFrost network as a new tissue collector on the criteria set in Annex I.

17. The Steering Committee will provide technical advice and coordination to the new collector institutes.

18. The Steering Committee will get in contact with collector institutes with requestors and to influence the agreement between the requestor and the collector institutes by offering standard consortium transfer agreements (Annex II).

19. The Steering Committee will inform the collector institution which other requestors are approached for the same proposal. Hence, they can communicate with each other on the subject of the proposals.

20. Complaints regarding the issue of tissue, excesses and non-compliances of the signed TuBaFrost Tissue Transfer Agreements will be handled by the Steering Committee.

21. The Steering Committee will update the European Human Frozen Tumor Tissue Bank Network strategy according with the new knowledge.

Chapter 4.2: *For all participants*

22. The routine diagnostic or prognostic use of the samples will be prioritized over the research use of the samples.

23. All participants will adopt the standardized work plan provided by the TuBaFrost consortium for ensuring the adequate management of the samples in terms of collection and storing as well as in the ethical and legal aspects of the clinical management of the samples.

24. Each member of the European Human Frozen Tumor Tissue Bank Network will prepare an annual progress report that will submit to the Steering Committee.

25. All collectors must communicate immediately the loss of availability to the central database if a sample is no longer available to TuBaFrost the European Human Frozen Tumor Tissue Bank Network.

Chapter 5:
Rights of all participants concerning the use of the European Human Frozen Tumor Tissue Bank Network

26. The members of the European Human Frozen Tumor Tissue Bank Network will have priority for the use of the services/samples of the network.

27. The members of the European Human Frozen Tumor Tissue Bank Network will have the possibility of personnel interchanges between participating institutions as well as training courses in histopathology and related techniques.

28. The members of the TuBaFrost consortium will participate in the co-authorship of the European Human Frozen Tumor Tissue Bank Network related publications.

29. Allocating part of the budgets of research projects using stored tissue, to the concept of management of samples of TuBaFrost the European Human Frozen Tumor Tissue Bank Network will be considered.

30. ***Acknowledgement policy.*** If results obtained with tumor tissues from European Human Frozen Tumor Tissue Bank Network results in a publication, the following statement should be included in the Acknowledgements or Material and Methods section of the manuscript: "*The tissue used in this publication was provided by TuBaFrost the European Human Frozen Tumor Tissue Bank*". In case facilities were used from the collecting institute(s), beyond the sole activity of issuing tissue, which in addition have contributed to a publication, the persons involved need to be treated as co-author of that publication.

Chapter 6:
The tissue request process (See Annex III for schematic representation)

As indicated introduction and point 4 of this policy report, the samples available in the European Human Frozen Tumor Tissue Bank Network will remain at the collector institutes. Hence, the authority and responsibility for the tissue falls under the collector and the final decision as to the destination of the stored tissue will remain with the collector institutions. This means that collector institutions will need enough information (by means of a tissue request form) regarding requestors and their research proposals to decide whether to provide the stored tissues.

31. The *tissue request form* (TRF) must provide enough information for collector institutions regarding requestor institutions and research proposals in order to facilitate their choice for the use of the stored tissue.

32. In the virtual tumor bank central database (Central Database), tissues can be searched and selected. A shopping cart as used by many Internet shops will mediate the selection of tissue. In the case of ordering frozen tissue a more appropriate name is chosen, the shopping cart is called "cryo-cart".

33. The TRF will be a web-based form for the requestor institutes, which will be presented when the contents of the cryo-cart is requested. The TRF is to be incorporated in WP 4.

34. Once these forms are completed and submitted to the Central Database, the system will automatically generate e-mails to the Steering committee and the collectors involved in the request (recognized using the TuBaFrost tissue ID). The collectors will use the information, on the form, to decide whether to participate in the research proposal.

35. The TRF will include the following items:

i. ***Principal Investigator.*** Already known from registration on the web site and login procedure and will be automatically added to the request mail.

ii. ***Requestor Institute.*** Full address.

iii. ***Number of samples necessary to carry out the research proposal***. In order to avoid requestors asking for more tissues than they need. This item will limit the amount of samples that can be added to the cryo-cart.

iv. ***List of chosen samples***. The requestor will use the search engine to select those stored samples of interest. The search engine will incorporate the "cryo-cart" option to be included in the web based TRF. The TuBaFrost ID will identify the samples.

v. ***Description of the research project and experiments to be performed***. This field is restricted to 250 words and must be in English. The requestor will have the possibility to upload a pdf version of the research project (at the same time as completing the tissue request form).

vi. ***Acquired approval of the Local Medical Ethics Commission or Multi-centre Research Ethics Committee,*** whenever is necessary according to regulations applicable to the requestor institute. This item will appear in the TRF as a YES or NO question.

vii. ***Number of the approval of the Local Medical Ethical Commission MEC or Multi-centre Research Ethics Committee MCREC***.

viii. ***Address of the Local MEC or MCREC***.

ix. ***Comments of the Local MEC or MCREC***, when available.

x. ***Is additional clinical patient data required?*** With this item in the TRF, the requestor will inform the collectors of the need of additional data on requested samples once the experimental study has begun. As the on-line tissue data-entry method is going to be used, the additional information can be updated in the tissue record on the Central Database system. The TuBaFrost Consortium recommends that the requestor should be informed of

the possibility of acquiring additional data before the collector gives their samples.

xi. ***Research activities of the requestor:***

1. ***Publications in the last five years*** (only the five most important).
2. ***Most relevant publications related to the project research*** (only the five most important).
3. ***Summary of the scientific activities***. The knowledge of the scientific activities of other institutions might open up the possibility of future collaborations between collector and requestors, including those not related with the proposal of the project.
4. ***Others.*** Any other information that the requestor thinks important or relevant for the collector to make a choice.

xii. ***Expected benefits derived from investigation***

xiii. ***Is there any possibility that the project will lead to a patent application or is it part of a larger project aimed at a patent application?*** If YES, TuBaFrost Consortium recommends an extended tissue transfer agreement between the requestor and all collectors implicated in the research proposal, covering the patent expected.

xiv. ***Financial support for the project indicating the financing bodies: government, pharmaceutical industry, private funds, others***.

36. The requestor institutes will receive a TuBaFrost number for their requests and they can follow the progress of the request on-line.

37. The collector institutes, which have been requested to issue tissue, get the opportunity to consult the TuBaFrost collectors, which are also involved in the same request in order to take an adequate decision. Therefore, the e-mail generated to the collector implicated in the tissue request will include the e-mail address and the contact names for all those collecting institutions implicated in the same request.

38. The time for the collector's decision is one month, if, however, more time is needed the requestor should be notified.

39. Once the collector has taken the decision concerning the request, they will inform the requestor, and also the other collectors involved in the request and the TuBaFrost Steering CommitteeThe TuBaFrost Steering Committee will provide a TuBaFrost transfer agreement, which can be used in the tissue transfer, and a recommendation for adequate frozen tissue transport through the TuBaFrost web site.

40. As specified in the TuBaFrost transfer agreement (Annex II), the requestor will commit to acknowledging TuBaFrost in any future publication AND requestor will inform the TuBaFrost Steering Committee about any subsequent publications (including congress communications) using tissue/data provided by TuBaFrost.

41. The TuBaFrost Steering Committee will publish the links of the publications prepared with TuBaFrost tissues, with the honorable mention of the collectors involved on its web site.

Chapter 7:
Recommendations for sample transport between collector and requestor institutes.

42. Transport of banked tissues between collector and requestor institutions must guarantee the quality of the frozen samples and falls under the agreements made between collector and requestor.

43. The collector institutes will be responsible for organizing the sample transportation to the requestor institute. However, the requestor will assume the total costs.The TuBaFrost Steering Committee will offer information regarding specialized companies through its web site. All these companies should offer specialized services for medical or bio-products transportation.

44. The TuBaFrost Consortium recommends isothermal boxes containing dry ice for sample transportation between collector and requestor institutes. The quantity and quality of the dry ice should be sufficient to guarantee the good preservation of the frozen samples during the time of transport. Alternatively an agreement between the transporter and the collector can be made on refilling the dry ice after certain periods of time.

45. The TuBaFrost Consortium recommends that the minimum time for the transportation of samples will always be less than 72h and the collector institutes will keep in mind that samples should not be sent on Friday due to weekend post not existing in most countries.

46. The container must be provided with a warning indicating that, although the TuBaFrost network attempts to avoid supplying tissues contaminated with highly infectious agents such as hepatitis and HIV, all tissues should be handled as if potentially infectious.

47. Banked samples will be transported in clearly marked cryovials on which the TuBaFrost tissue ID must be perfectly readable.

48. Each sample should be mentioned on an enclosed datasheet together with the minimal dataset. The collector can print this out from the online central database and send it together with the material, or the researchers will be able to view or print out this minimal data set directly from the central database online.

49. The collector and requestor institutes will have the possibility of submitting a problem feedback report to the TuBaFrost Steering Committee and the involved collectors. This report will be online based and will contain the following items:

1. Request Number.
2. TuBaFrost code for each sample.
3. Requestor and collector institutes involved, with contact names.
4. Principal researcher.

5. Date of request.

6. Clear description of the problem.

Chapter 8:
Quality control

50. Quality controls must be applied to each local tumor bank participating in the TuBaFrost network by means of what is decided in WP 3.

51. The TuBaFrost Steering Committee will make these rules available on the TuBaFrost web site.

52. The data accompanying the samples on transfer will be at least the data sent to the central database. In addition, all data supplied will include the TuBaFrost ID. The collector, on agreement between collector and requestor, can supply other non-identifying data coupled to the TubaFrost ID number.

53. The TuBaFrost Steering Committee is authorized to ask collectors for an evaluation report on quality issues, or even audit collector institutes on suspicion of not following the quality control procedures based on submitted problem. However, TuBaFrost Steering Committee merely mediates and provides guidance with respect to the quality of the tissue and the exchange program in general, but is not responsible for the quality of the tissue or data provided to the requestor.

54. In case the quality control appears to be not up to standard and no improvement in quality control is to be expected, the TuBaFrost Steering Committee can stop collaboration with the collector. The decision to stop collaboration with a collector will be made by the TuBaFrost Consortium as a whole.The TuBaFrost Central Database system will have an online tool that allows the central office to monitor quality control programs.

Annex I:

Criteria for collector institutes for participation in Tubafrost the European Human Frozen Tumor Tissue Bank Network

1. All collector institutes must have the availability and access to cancer patient specimens.

2. Collector institutes must have the availability of sufficient personnel (technicians, pathologists, etc) and infrastructure capacity for the development and/or maintenance of a tumor bank, which meets the minimal standards and can collect tissue according to the protocols and rules set by the European Human Frozen Tumor Tissue Bank Network.

3. In order to participate in the European Human Frozen Tumor Tissue Bank Network all or potential collector institutes will establish a tissue bank, collect specimens and corresponding clinical data according to the standardized collection methods and policies of the European Human Frozen Tumor Tissue Bank Network in order to assure quality control of specimens and data.

    a. The collector institutes will name a member of the institute as a responsible of the scientific tasks of the tumor bank (macroscopic analysis, and selection and harvest of the surgery specimens). Those selected persons should demonstrate their interest in participating in the tumor bank and cancer research. He/she will be responsible of the functional aspects such as reception, processing and storing of the samples, quality controls, legal and ethical aspects, management of the information referred to each sample and the distribution of the samples.

    b. The collector institutes should have a technician responsible for the processing, storing and cryo-preservation of the samples.

    c. The collector institutes will indicate the existence of a budget, a physical space and equipment to perform the activities of the tumor bank.

4. The collector institutes are responsible for the association of samples with valid consent to ensure legal research use of TUBAFROST material by the requestor institutions.

5. The collector institutes will be required to accept and implement the common policies and procedures approved by the TUBAFROST consortium (or the Steering Committee).

The collector institutes will be required to accept the cooperative action between the tumor banks of the European Human Frozen Tumor Tissue Bank Network.

Annex II:
Consortium transfer agreement a standard model for ratification of the final agreement between collector and recipient

TUBAFROST TISSUE TRANSFER AGREEMENT

1. **Definitions:**
   a. Provider: A collecting member of the TuBaFrost, the European Human Frozen Tissue Bank, which provides the tissue as specified in the TubaFrost request form.
   b. Recipient: An organization which has requested tissue from the TubaFrost repository.
   c. Collecting member: An organization, which is participating in the TubaFrost by collecting tissue and making tissue available according to the procedures of TubaFrost.
   d. Tissue: Human biological material taken from patients in the course of a clinical procedure or specifically taken out in order to be used for research purposes.
   e. The tissue Tissue which is provided by provider to recipient following the request form and this Agreement
   f. Research: Scientific research on tissue and related data not involving the use of tissue in human subjects.
   g. Donor: The patient form which the tissue originates
   h. TubaFrost: The European Frozen Tissue Bank as defined (legal entity to be determined).

2. Obligations of provider
   a. Provider will provide the tissue and related data as described in the request form as far as possible
   b. Provider will notify recipient as soon as possible if providing the tissue and/or data meets obstacles, like (but not limited to) the tissue is needed for further diagnostic procedures for the donor, the tissue has become unavailable or has become unsuited for the requested use due to unforeseen circumstances, the tissue can not be shipped of exported due to applicable regulations.
   c. Provider will only provide tissue and related data which may be used for the research as specified in the request form according to the regulatory and ethical standards applicable to provider

3. Obligations of recipient
   a. The tissue and data will only be used for research as specified in the request form
   b. Recipient will only use the tissue if so allowed by the regulatory and ethical standards applicable to recipient
   c. No attempts whatsoever will be made to find the identity of the donor or to derive other data form the tissue as follows from the research described in the request form.
   d. Tissue and their derivates shall not be sold, or distributed free of charge to third parties, and can only be used to produce commercial medical products (including the production of cells or cell products for sale) in collaboration and with written permission of the provider and proper consent of the patient.
   e. Recipient will bear the costs of preparing the tissue as requested in the request form and of handling and shipping the tissue to recipient
   f. After performing the agreed research the remaining tissue and their derivates will be returned to provider. The recipient agrees to assume all risks and responsibilities in

connection with the receipt, handling, storage, use of the tissue and return shipment of the remaining tissue.

g. The recipient will pay to the TubaFrost consortium the costs as set in its rules of procedure for its mediation between provider and recipient.

4. General clauses

a. Recipient understands that while provider attempts to avoid supplying tissue contaminated with highly infectious agents such as for instance hepatitis and HIV, all tissues should be handled as if potentially infectious. The recipient acknowledges that he is aware of and follows applicable regulations for handling human specimens and will instruct its staff to abide by those rules. The recipient further agrees to assume all responsibility for informing and training personnel in the dangers and procedures for safe handling of human tissues.

b. The tissue is provided as a service to the research community without warranty of merchantability or fitness for a particular purpose, including that which is described in the request form, or any other warranty, express or implied.
Provider nor the Tubafrost consortium can be held liable to recipient for any loss, claim or demand made by recipient, or made against recipient by any third party due to or arising from the use of the tissue by recipient, except to the extent permitted by law when caused by gross negligence or willful misconduct by provider.

c. The recipient hereby agrees to acknowledge the contributions of the European Human Frozen Tumor Tissue Bank (Tubafrost) in all publications resulting from the use of these tissues. Recommended wording to the Acknowledgment or Methods section is as follows: "*The tissue used in this publication was provided by Tubafrost, the European Human Frozen Tumor Tissue Bank Network*". In case facilities or services were used from the collecting institute(s), beyond the sole activity of issuing tissue, which in addition have contributed to a publication, the persons involved need to be treated as co-author of that publication.

d. The undersigned warrant that they have authority to execute this agreement on behalf of respectively provider and recipient.

Name of Recipient

_____

Division or Department

_____

Institution _____ **Date** _____

Place

_____

Function of Recipient

_____

Signature of Recipient _____

Name of provider

_____

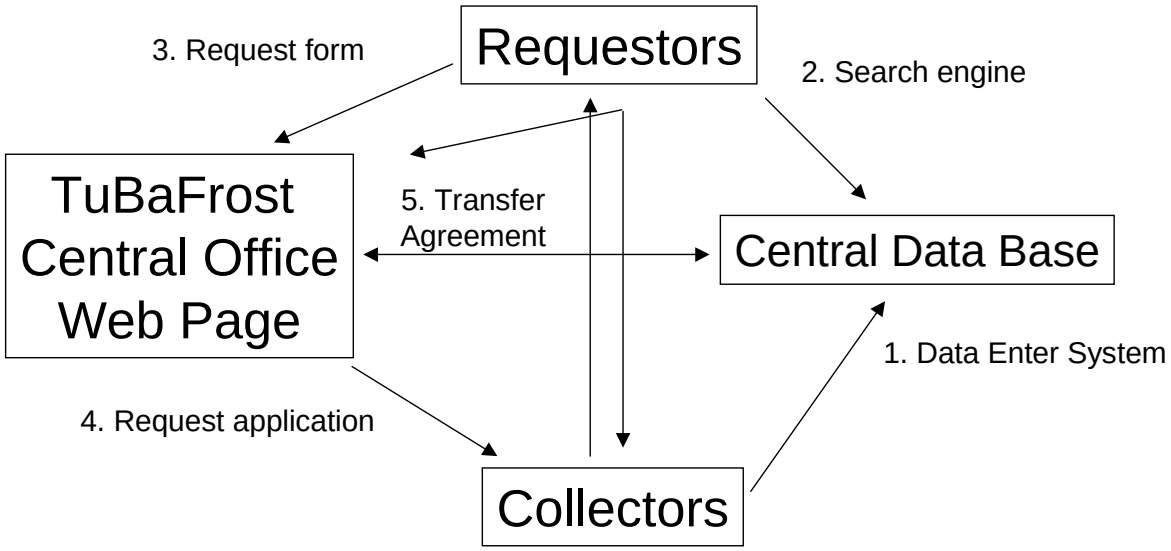
Division or Department
_____

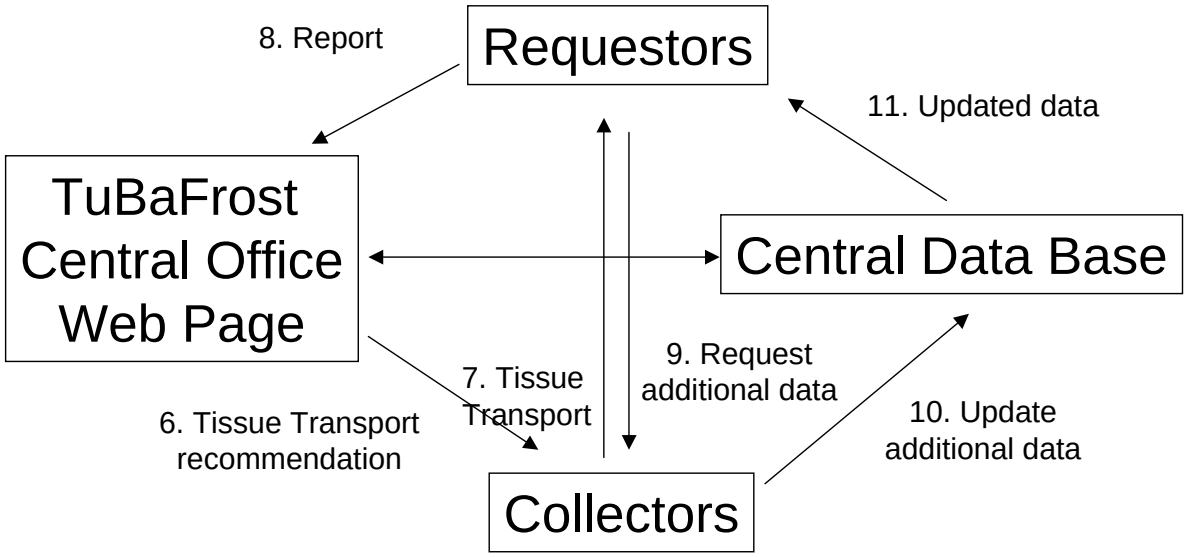
Institution **_____** **Date** **_____**

Place_____

Signature of Provider
_____

Annex III:
Schematic Diagram of the Tissue Request Process.





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