



Ethical charter on the collection, storage and use of human tumour samples for therapeutic or cancer research purposes

Guidelines for medical practitioners, researchers and managers of tumour banks and biological resource centres

The purpose of this charter is to facilitate cancer research. It has been drawn up to guarantee ethical conduct and protect the rights of patients in interactions between health care facilities, tumour bank management units or biological resource centres (BRCs) and researchers.

However, this is not the charter's sole objective. It will also ensure that medical practitioners with access to tumour banks or BRCs are better informed of rules and regulations regarding patients' rights.

Hence patients and society in general will ultimately benefit from the ethical practices described herein.

Context and purpose

Human biological resource centres have gradually taken on an essential role in biomedical research structures, in a context where our understanding of biological mechanisms is subordinated to our knowledge of molecular processes and structures and, in particular, the biological regulation mechanisms governed by the human genome [1]. Cryopreserved tumour banks (also known simply as tumour banks) play an important role in cancerology. Firstly, these banks are a clinical necessity given the emergence of new classifications based on the genomic properties of tumours [2-3] and the development of targeted treatments requiring the identification in the patient of molecular markers specific to the action mechanism of these treatments [4-7]. Secondly, tumour banks are an essential resource for research programmes on cancer biology. In view of this dual objective, tumour banks are at the interface between research and treatment, and as such are emblematic of the current challenge to develop research and hence discover new mechanisms of therapeutic action against cancer. This specific feature of tumour banks is reflected in the sample collection process, which is based primarily on the storage of specimens removed surgically as part of a treatment programme, rather than on the collection of tissues removed specifically for the purposes of a research programme.

Of course, the quality of preserved samples, which is absolutely essential to RNA and proteomic analysis in particular, is governed by a set of national technical guidelines [8-10]. However, in addition to this, the use of human body parts for research purposes raises a number of legal questions relating to the protection of individuals [11-13], as well as some ethical issues [14,15] that are not all covered by the August 2004 version of the French law on bioethics.

On an international level, these questions have been the subject of several agreements and guidelines for governments [16-18].

Various work groups or reports have already contributed significantly to these questions by conducting analyses and issuing opinions [19, 21]. The French National Federation of Anti-Cancer Centres has produced a practical guide to the use of tumour tissue in biomedical research, which discusses the specific characteristics of tumour banks [22]. However, at present, there are no legally up-to-date reference texts to govern and facilitate the use of tumour banks for biomedical research purposes. This charter, drawn up by the French National Cancer Institute, is intended to fill this gap.

The purpose of this charter is to help further one of the main objectives of the French national cancer plan 2003-2007 [23]: to increase the ability of medical research institutions to generate progress that can very quickly be put into practice on cancer patients. This charter should enable clinicians, researchers and managers of hospitals and research units to enhance the role of tumour banks in research programmes (including joint public/private programmes) while protecting patients' rights and adhering to ethical standards and national and international regulations. It defines, through five very straightforward recommendations, a set of principles that will both protect patients' rights and further the respective objectives of researchers and doctors.

Development method

The French National Cancer Institute invited a group of legal experts and anatomical pathologists headed by Professor A. Janin (see appendix 6) to analyse existing legal texts, and any published or unpublished guidelines, reports or studies in France relating to tumour banks. It also asked the group to examine scientific publications on legal issues and ethics, which could be used in the French context.

This work group has issued recommendations and, whenever necessary, has provided explanations on how best to implement them.

A second work group was set up by the French National Cancer Institute and the LEEM (the French trade organisation for pharmaceutical companies) (see appendix 7). This group consisted of jurists and research managers from various pharmaceutical laboratories. It identified the conditions conducive to the development of public/private research partnerships. Above all, this group addressed the questions of issues and the sharing of rights, and discussed the specific legal constraints on multi-national corporations (exporting samples, jurisdiction).

Whenever a consensus could not be reached, either within one of the groups or between the two groups, the solution chosen was that which provided the greatest protection of individual rights.

The entire charter project was then submitted to a large panel of revisers including independent bodies, institutions and learned societies (see appendix 8).

CHARTER

RECITALS: any organisation wishing to store and prepare human body parts for the purposes of its own research programmes, or create and use a collection of human biological samples, must notify the relevant authorities beforehand¹.

Article 1:

Where a human tumour sample (tissue, cells, blood) is collected as part of a treatment procedure and stored for biomedical research purposes, part of the tumour (tumour specimen) shall, whenever possible, be kept for the individual benefit of the patient.

Article 2:

Human tumour samples shall not be used for any other medical or research purpose than that for which they were initially collected, unless the following two conditions are both met:

- The patient has been informed beforehand of the new purpose
- The patient has not objected to the new purpose

Where the use of a tumour sample is likely to require an examination of the patient's constitutional genetic information, then the patient must:

- be informed beforehand of the nature and purpose of the said examination
- give his or her express consent

Article 3:

All information, lack of objection and consent documents shall be kept in the patient's medical file.

Article 4:

Where human tumour samples collected during diagnostic or medical examinations are used by one or more third parties for research purposes, a partnership agreement shall be drawn up with the health care or research facility responsible for the samples. This agreement shall clearly state the objectives of the research programme. It may relate to a straightforward partnership or to a joint research programme.

Human samples collected during diagnostic or medical examinations shall not be given or sold to a third party unless such an agreement has been drawn up. Exclusive rights shall not be conferred under any circumstances whatsoever.

Unless otherwise stipulated, human tumour samples shall not be supplied to researchers in native conformation. They shall be delivered in the form of quality-controlled derivative products, in pre-defined quantities and for a specific research programme. Under no circumstances shall any surplus material or personal information relating to the samples be re-used for a research programme other than that originally stipulated.

A signed contract shall define the relationship between the parties and specify the rights and obligations of each partner. Hence a climate of confidence can be established.

Article 5:

Human tumour samples used for research purposes may be accompanied by directly or indirectly nominative data that is processed electronically. In this case, the necessary formalities must be completed with the national data protection authority (CNIL).

In the case of a joint research programme, the transfer of directly or indirectly nominative data shall comply with strict regulations.

¹ This notification must be submitted to the Ministry of Research and must be accompanied by a statement of opinion from the Ethics Committee. If the organisation in question is a healthcare facility, the declaration must also be submitted to the director of the locally competent ARH (hospital management agency) (see article L.1243-3 C of the Public Health Code).

ARTICLE 1

Where a human tumour sample (tissue, cells, blood) is collected as part of a treatment procedure and stored for biomedical research purposes, part of the tumour (tumour specimen) shall, whenever possible, be kept for the individual benefit of the patient.

OBSERVATIONS

This article is an ethical recommendation specific to this charter

A survey of recent medical literature [24-26] shows the emergence of new anti-tumoural treatments targeting the specific biological properties of tumour cells and tissues.

Hence, in some cases, it is necessary to identify these biological properties in order to be able to predict the effectiveness of tumour-targeted therapies. To do this, tumour tissue of all types must be stored in paraffin blocks. For some tumour types, the cryopreservation of tissues, cells and/or blood and plasma is also required (cf. future INCa guidelines for the cryopreservation of tumour samples collected for therapeutic use).

Furthermore, samples collected for treatment purposes and stored in tumour banks must be made available for medical research programmes, on the condition that the patient has been informed and does not object (cf. article 2). Human tumour samples may also be stored specifically for research purposes, whether they were collected for treatment purposes or for a particular research protocol.

However, in regard to samples collected during treatment and used for research purposes, it is good medical practice to keep a fragment of the initial tumour² whenever possible, in case a new targeted therapy is discovered. This is in the potential interest of the patient and applies as long as the patient is alive. The analysis of the biological properties of this fragment may, in some cases, provide solid grounds for proposing a new course of treatment.

Note:

- Sampling and storage procedures must, of course, comply with the bioethics principles set forth in the Civil Code and the Public Health Code (see p. 14 of this charter).
- European Directive no. 2004/23 of 31 March 2004 deals with the development of quality and safety standards relating to the donation, collection, inspection, processing, storage and distribution of human tissues and cells.
The principles set forth in this charter comply with this Directive, especially in regard to guaranteeing data protection, traceability and confidentiality.
- In 2000, the ANAES (French National Agency for Healthcare Accreditation and Evaluation) issued guidelines on the cryopreservation of tumour cells and tissues for purposes of molecular analysis. These guidelines can be viewed on the National Health Board's website (www.has.sante.fr).

² Any storage method may be used, for example a paraffin block or cryopreservation.

ARTICLE 2

Human tumour samples shall not be used for any other medical or research purpose than that for which they were initially collected, unless the following two conditions are both met:

- The patient has been informed beforehand of the new purpose
- The patient has not objected to the new purpose

Where the use of a tumour sample is likely to require an examination of the patient's constitutional genetic information, then the patient must:

- be informed beforehand of the nature and purpose of the said examination
- give his or her express consent

OBSERVATIONS

This article reflects current legal regulations and recommendations.

1. The public health code sets out, as a general principle, that the **removal** of human body parts or the collection of human products from an **individual may not be performed without the prior consent** of the said individual, and that this consent may be withdrawn at any time.

Art. L.1211-2 par. 1 of the Public Health Code: "*The removal and collection of human body parts and products may not be performed **without the prior consent of the donor**. This consent may be revoked at any time*".

Nevertheless, if the parts were removed or collected for diagnostic or treatment purposes, but a practitioner wishes to store them and use them for another **medical or scientific purpose**, the law stipulates that the further use of tumour samples is possible, unless the patient:

- who has been duly informed beforehand of this new purpose,
- objects to this new purpose.

Art. 1211-2 par. 2 of the Public Health Code: "... *the use of human body parts or products for a medical or scientific purpose other than that for which they were removed or collected is possible, **unless objected to by the person from whom these parts or products were taken, who was duly informed beforehand of this new purpose**...*"

Moreover, there are two international texts dealing with patients' rights and ethical issues relative to the use of human body samples: the Oviedo Convention, signed by France in 1997 [17] and the recent European Council recommendation of 15 March 2006[18]. These two texts recommend applying the principle of "appropriate consent", with regard to the use for research purposes of biological samples collected during treatment. The recommendation issued in this charter, in application of the bioethics law, is based on "the lack of objection from the duly informed party". This is perfectly consistent with the above-mentioned international recommendations, provided that the said party is informed in an appropriate manner, according to the provisions in this charter³.

A standard patient information document is provided in appendix 1.

³ Article 22 of the Oviedo convention, which France signed on 4 April 1997, and article 12 of the European Council recommendation of 15 March 2006 stipulate that the use for research purposes of biological samples collected during treatment requires appropriate consent or authorisation. The law on bioethics of 9 August 2004 stipulates that the duly informed patient must not have objected to such practice. In this respect, the present charter is perfectly compatible with the European Council recommendation: it stipulates that the patient must be informed in person by a health professional, that a written explanation must also be given to the patient during the meeting and that the health professional must ensure that the patient does not wish to raise any objections. The health professional must then draw up a signed and dated statement to this effect on a copy of the information document kept in the patient's medical file. This point was discussed, assessed and approved in August 2004, when the law on bioethics was voted in; it was also discussed with and approved by the European Council's bioethics department, which coordinated the recommendation of 15 March 2006.

Box 1. Focus on:

Best practice relative to informing a patient on the use of samples for a purpose other than diagnosis or treatment, and ensuring that the said patient does not object to this new purpose.

◆ The practitioner, who wishes to store human body samples (for example in a tumour bank) and use them for another medical or scientific purpose, must:

- **inform the patient of this new purpose.**

The patient may be informed before or after the sample is taken. The information must be delivered by a doctor or by a health professional who is able to give further explanation to the patient if necessary.

It is up to the medical team to choose the most appropriate time: during the pre-surgery or pre-anaesthetic consultation, during the patient's stay in the healthcare facility, after the operation, when the patient is ready to go home, etc. The most appropriate time is when the patient is least likely to be upset or disturbed by the information and the most likely to understand it, given that he or she is already burdened with a lot of administrative and medical formalities. Attention is drawn, in particular, to the importance of verbal explanations. A written document on its own is not sufficient.

In any case, the information provided explains the objectives pursued, the scientific benefits of such research and the results that may be expected of it. Of course, it does not go into the details of the specific research programme(s). The patient should also be told where the sample will be stored and what it is expected to be used for. The written information document should mention the name of the storage facility and of the storage team manager, and should specify that the patient may personally benefit from the sample during subsequent treatment.

- **Make sure the patient does not object to the subsequent use of the sample.**

The Public Health Code does not, in the case in point, require written consent from the patient. It is up to the practitioner and, more broadly speaking, the medical team to ensure that the information provided is accurate and that the patient does not wish to raise any objections. Patients must be given enough time to think things through, ask questions, express their concerns and, if necessary, their opposition.

To avoid future disputes, it is advisable to:

- Draw up an information document, give one copy to the patient (cf. appendix 1) and put another copy in the patient's medical file. It is also possible to give a copy to the tumour bank management unit.
- Stipulate in the patient's medical file that "*the patient has not raised any objections to the subsequent use of the sample*" and that "*an information document was given to the patient on (date)*". Details of patient interviews should also be given.

NB: it may be useful to write these statements on the copy of the information document kept in the patient's medical file, as suggested in appendix 1.

◆ **Several successive cancer research studies may be conducted, provided that the objective of these studies is in line with the information given to the patient. It is a different matter if substantial changes have been introduced: type of research, different speciality, etc.**

2. The use of samples in “**examinations aiming to define the constitutional genetic information** of an individual” requires formal consent. The patient must give his or her “express”, i.e. written, consent and must be duly informed beforehand of how the samples will be used and for what purpose;

Art. 16-10 of the Civil Code: “A person’s genetic information may only be examined for medical⁴ or research purposes.

The express consent of this person must be obtained beforehand, once he or she has been informed of the nature and purpose of the examination.

The consent document must mention the purpose of the examination. It can be revoked at any time.”

The term “constitutional genetic information” refers to the hereditary genome, whereas the DNA analysis of tumour samples identifies mutations in the somatic genome and enables the creation of a tumour “identity card”, which is essential to defining a treatment programme and establishing a prognosis⁵.

Note: the regulations on genetic examinations will soon be completed, when article R.1131-1 is updated in application of articles 5 and 6 of law no. 2004-800 of 6 August 2004 (drawn up in January 2006).

This genetic examination, which focuses on the specific characteristics (constitutional genetics) of an individual, requires the patient’s consent. This consent must be in **written** form and **signed** by the patient.

A document is given to the patient, specifying:

- what the examination consists of: type of analysis, technique used, etc.
- the purpose of the examination: medical or research objectives.

The chief doctor must determine the best time during which to approach the patient to obtain written consent. He or she must also decide who is the most qualified to deliver the appropriate information.

Practitioners who conduct a genetic examination for medical purposes must be authorised to do so by the Biomedical Agency (art. L. 1131-3 of the Public Health Code).

An example of the information document given to the patient is provided in appendix 2.

Box 2. Focus on:

The procedure to be followed for re-using biological samples collected prior to the law on bioethics of 6 August 2004, or taken without the patient’s knowledge and therefore without giving the patient an opportunity to object.

- The new rules apply: the samples can be used unless the patient, on being informed of this use, decides to object.
- There are **two exceptions** to the principle of prior information:

⁴ The examination of genetic information for medical purposes is defined as follows in the Public Health Code:

Art. R.1131-1 of the Public Health Code: “The examination of a person’s genetic information for medical purposes serves to:

- either confirm or invalidate the diagnosis of a genetic disease in a person presenting the symptoms of this disease,
- or identify, in an asymptomatic person, the characteristics of one or more genes that are likely to lead to the development of a disease in this person or in his or her descendants.”

⁵ Definition suggested by the Academy of Medicine.

1. Where the person cannot be found, because he or she is deceased or for any other reason. In this event, the law allows the sample to be kept and used, even though the person has not been informed.

Art. L.1211-2 par. 2 of the Public Health Code: “... *the obligation to inform may be waived in the event the person concerned cannot be found...*”

2. Where the research manager refers the case to the Ethics Committee and this committee decides that it is not necessary to inform the person concerned (see page 13).

It should be noted that in the particular event that the studies conducted are likely to include an examination of the patient's genetic information, written consent is required (see page 9).

In practice:

- It is advisable to **contact the patient** to inform him or her of the collection and storage of the samples and of the plans to use them. The patient should also be informed that he or she is entitled to object to these plans.
- **When the patient cannot be found**, the chief doctor must make sure that it really is impossible to find the patient and must add all information to this effect to the medical file. This may include information obtained by telephone (the record of the call, and the name and details of the correspondent, must be signed and dated) – or by letter or e-mail (notification of death, letter returned by the post office, showing that the person has moved away without leaving a forwarding address, etc.).

However, the obligation to inform the person concerned may not be waived if the samples collected include **germinal tissues or cells**. In this case, if the person is deceased, it is forbidden to use the samples for any other purpose than that originally intended.

Art. L. 1211-2 par. 2 of the Public Health Code:
“Nevertheless, this waiver is not permitted if the samples taken consist of germinal tissues or cells. In this case, should the interested person be deceased, it is forbidden to use the samples for any other purpose than that for which they were originally taken”.

Box 3. Focus on:

The procedure to be followed for re-using biological samples taken from a minor or an adult under guardianship.

In this case, the same rules apply, but the information must be given to the persons holding parental authority or to the guardian. The latter are the only persons entitled to file an objection.

Of course, much more time and attention are required when informing the parents of a minor. It is always difficult to inform a mother and father in such a situation. Their anxiety and distress should be kept in mind at all times.

The child may also be made party to the information and involved in the decision-making process, provided that he or she seems sufficiently mature and that it is done in the most appropriate manner possible (art. L. 1111-2 of the Public Health Code)⁶.

⁶ Should the research programme require not only the tumour sample but information on the fate of the minor, all possible effort shall be made to inform patients who have come of age since the sample was collected.

3. If, when the sample is taken, the patient is included in a biomedical research study:

The patient may, when the sample is taken, be included in a biomedical research study “organised and conducted with a view to furthering biological and medical knowledge”. In this case, the study is subject to ethics laws designed to protect people participating in biomedical research (art. L. 1121-1 to L. 1126-7 of the Public Health Code).

There are **three possible scenarios**:

1. The sample is taken from the patient for diagnosis or treatment purposes, and not for research. All actions are performed and all products are used normally. No additional or unusual diagnosis or monitoring procedures are implemented for research purposes.

In this case, the above-described standard procedures apply: the patient must be informed beforehand and must not object to the sampling procedure.

2. The use, for research purposes, of samples collected during diagnosis or treatment is provided for right from the start in the biomedical research protocol.

3. Sampling is directly provided for in the research protocol.

In these last two cases, the provisions of the public health code relating to biomedical research apply: **the use of particular samples for research purposes must be fully explained to the patient, along with all the other information provided by the attending investigator or doctor.** This must be done before the research begins; the patient’s **written consent** to the research must be obtained (art. L.1122-1 and L.1122-1-1 of the Public Health Code).

Moreover, the patient must be informed beforehand of any plans to re-use the samples for new research, and he or she must not object to this further use (cf. 1st paragraph of article 2).

The information document given to a patient within the framework of a biomedical research project can also be used to inform this patient that samples may be re-used for new research in the future and that he or she is entitled to object to such further use.

This obligation to inform may only be waived if the advisory ethics committee consulted by the research manager judges that it is not necessary (art. L. 1211-2 par. 2 of the Public Health Code) (see box 2). However, as stipulated above, this waiver is not permitted if the samples originally collected consist of germinal tissues or cells.

Article 3

All information, lack of objection and consent documents shall be kept in the patient's medical file.

OBSERVATIONS

This article is a legal recommendation specific to the charter.

1. **As mentioned above, an information document is drawn up** (see box 1). It may or may not be signed by the patient, depending on the circumstances:
 - information on a sample and the proposed use of this sample, excluding any examination of genetic information: document not signed by the patient (appendix 1)
 - information on a sample and the proposed use of this sample, including an examination of genetic information: document signed by the patient (appendix 2)

Of course, the interview or interviews with the patient are recorded in his or her medical file.

A copy of the information document is put in the medical file. Hence the information document must comprise two identical sheets. One is given to the patient; the other is kept in his or her file. Both sheets have the date on them. The line specifying if the patient objects or not must be completed (unless the patient's genetic information is to be examined). The two sheets clearly indicate the name of the health professional who conducted the interview. The copy kept in the medical file is signed by this person. If the tumour bank management unit so requires, it is provided with a copy of the information document as proof that the patient has been adequately informed.

If necessary, the patient's express consent is obtained and kept in the same file (if an examination of the patient's genetic information is intended).

In most cases, these documents are in electronic form. However, the patient's signature (when it is required) must either be handwritten or, in the case of an electronic signature, valid.

2. **The storage period** for these information and consent documents is the same as that for the other documents in the medical file.

Reminder of applicable storage periods, as stipulated in the decree of 4 January 2006 (R1112-7, Public Health Code) on the hosting of medical data (applicable as of 5 January 2007):

- medical files put together by healthcare facilities shall be kept for 20 years, as of the date of the patient's most recent stay in the facility or most recent visit as an outpatient;
- where the applicable storage period comes to an end before the patient's 28th birthday, the file shall be kept until this date;
- in all events, if the patient dies less than 10 years after his or her most recent visit to the facility, the file shall be kept for 10 years as of the date of decease.

According to article R. 1131-15 of the Public Health Code:

- 30 years for clinical pathology reports and conclusions, relating to the examination of genetic information.

3. **Should a third party in a joint research programme wish to verify the patient's consent or lack of objection**, a document devoid of any information identifying the patient

may be delivered to this party, certifying that the sample was taken in accordance with the legal procedures in force.

The healthcare or research facility in charge of the tumour bank may not give nominative information documents or consent forms to any third party other than the patient or tumour bank management staff. However, it may certify in writing that the tumour sampling procedure was compliant with legal requirements.

Access to information documents and consent forms is governed by the rules that apply to accessing medical records. Unless the documents are strictly anonymous, access is reserved to the following:

- the patient,
- the patient's legal representatives,
- the patient's assignees (provided that the patient has not, during his or her lifetime, registered an objection, assignees may be granted access for three purposes: to find out the cause of death, to defend the memory of the deceased or to assert their rights),
- the healthcare professionals responsible for the patient, for ensuring continuity of treatment or for defining the best medical care possible.

ARTICLE 4

Where human tumour samples collected during diagnostic or medical examinations are used by one or more third parties for research purposes, a partnership agreement shall be drawn up with the health care or research facility responsible for the samples. This agreement shall clearly state the objectives of the research programme. It may relate to a straightforward partnership or to a joint research programme.

Human samples collected during diagnostic or medical examinations shall not be given or sold to a third party unless such an agreement has been drawn up⁷. Exclusive rights shall not be conferred under any circumstances whatsoever⁸.

Unless otherwise stipulated, human tumour samples shall not be supplied to researchers in native conformation. They shall be delivered in the form of quality-controlled derivative products, in pre-defined quantities and for a specific research programme. Under no circumstances shall any surplus material or personal information relating to the samples be re-used for a research programme other than that originally stipulated.

A signed contract shall define the relationship between the parties and specify the rights and obligations of each partner. Hence a climate of confidence can be established.

OBSERVATIONS

This article is a legal recommendation specific to the charter

1. General principles apply

Several principles apply to a joint research programme:

- human tumour samples may only be removed or collected for therapeutic or research purposes (art. L. 1241-1 C. of the Public Health Code),
- neither the human body, nor any of its parts and products, may be the object of property rights (art. 16-1 C. of the Civil Code, principle of the unavailability of the human body),
- persons donating either body parts or products shall not, under any circumstances, receive financial compensation for doing so (art. 16-6, of the Civil Code),

Human tumour samples, which are not governed by property rights, may not become objects of trade.

⁷ Transfers outside the framework of the partnership agreement are not covered by this charter. Any organisation involved in processing and preparing human tissues and cells in view of giving them or selling them to a third party for research purposes (including genetic research) should request authorisation to do so from the Ministry of Research. Where this organisation is a healthcare facility, joint authorisation should be issued by the Ministry of Research and the locally competent ARH (art. L.1243-4 of the Public Health Code). The implementing decree for the bioethics law on the storage and preparation of human tissues and cells for research purposes, which is currently being drawn up, should confirm this principle. It should stipulate that the provision of samples within the framework of a specific research partnership is not considered a transfer, in the sense intended in article L1243-3.

⁸ In the particular case of samples collected for biomedical research, the promoter may of course enjoy exclusive rights for a period of time to be defined.

On the other hand, within the framework of a partnership agreement, the sample storage facility may define how the samples will be used by the receiving party. The partnership agreement must stipulate that the receiving party may not subsequently give or sell the samples to a further party.

2. The partnership agreement may take either one of two forms:

Form 1:

- A **straightforward partnership agreement**, whereby the manager of the tumour bank supplies a given quantity of biological material, but does not participate to any significant extent in subsequent research activities (e.g. validation of previously identified therapeutic targets).

This type of partnership agreement does not contain a valuation clause or confer patenting rights on the tumour bank management facility. On the other hand it does contain a financial clause, providing for the remuneration of this facility for services provided.

- Furthermore, this charter prohibits the transfer of biological material to a third party outside the framework of the partnership agreement, whether this transfer be paid or not. In all events, the tumour bank management facility must obtain authorisation from the Ministry of Research prior to any transfer.

Form 2:

- **The partnership agreement is more complex.** The tumour bank management facility and the third party set up a joint research programme. The parties enter into a more extensive partnership, whereby each party contributes to research activities.

This partnership is based on a set of joint objectives. Research teams from both organisations work together and share equipment.

If possible, the services provided by each party are identified when the agreement is signed and valued accordingly.

In all events:

It is essential that human tumour samples only be made available within the framework of a partnership agreement between the healthcare facility or public-sector research establishment (EPST) and the recipient party.

The terms of this partnership are set out in **a written contract or agreement** specifying, in particular:

- the legal context governing the field in question, and the necessity of adhering to the main principles of the Civil and Public Health Codes (as outlined above).
- the objective of the partnership. Regardless of the type of partnership, the agreement must contain a description of the research to be conducted on the biological material provided. The organisation entering into partnership with the tumour bank management facility must give an account of the studies that will be performed and the tests that will be conducted on the tumour samples.
- the terms and modalities of quality control, as applied to tumour samples.
- the storage, traceability and utilisation policies implemented by the third party.
- the confidentiality procedures implemented to protect patient data.

- the certification of the conditions under which patients were informed and indicated their consent or lack of objection.
- the amount of funds paid to the tumour bank management facility. Although the biological material itself may not be sold, the services provided by the tumour bank management facility (storage, referencing, maintenance, transportation, labour) must be evaluated and remunerated.
- the responsibilities (or lack of responsibilities) of each party, with regard to the delivery, the quality and the use of the biological material.
- the procedures for returning tumour samples (if necessary and in exceptional circumstances) to the supplier facility.
- contract termination procedures and possible grounds for termination.
- solutions for settling any disputes that may occur (mutual agreement procedure, jurisdiction, etc.)

Appendix 3 contains standard partnership agreements and lists the main items to be included in this type of contract.

3. A delivery slip or receipt, known as a Material Transfer Agreement (MTA), is drawn up for each delivery of human tumour samples.

Each transfer is accompanied by a Material Transfer Agreement (MTA) which clearly identifies the contents of the transfer. This document completes the above-described agreement. In the case of a straightforward partnership, it may be included in the agreement.

Appendix 4 contains the stipulations of the MTA, which may be either incorporated into the partnership agreement (for a straightforward partnership) or appended to it (for an extensive partnership agreement).

4. Procedures relative to the traceability and storage time of human tumour samples must be drawn up.

The tumour bank management facility must, when providing tumour samples to a third party, keep a record of the delivery conditions and of the third party that will be using the samples. This information must be entered into the management facility's information system or into a register designed specifically for this purpose. The recipient must sign the above-mentioned delivery slip or receipt (MTA).

Tumour samples delivered to a third party within the framework of a research partnership are kept for the duration of the research project. Any sample surplus remaining at the end of the project must be disposed of rather than returned to the supplier facility.

The recipient of the human tumour samples may not transfer them to a further third party.

5. Human tumour samples for research purposes must be delivered in the form of quality-controlled derivative products, in pre-defined quantities and for a specific research programme.

Cellular and tissue tumour samples are generally stored in native form. These samples may subsequently be used in the form of tissue cross-sections or "derivative products" such as DNA, RNA or proteins.

Thanks to progress in systematic screening, tumours are now smaller at the time of diagnosis. Furthermore, the original samples are more widely obtained by image-guided biopsy rather than by

surgical means. Therefore, the tumour material is often used entirely for diagnosis purposes, and the amount of biological material available for research protocols is more and more limited.

One way to achieve optimal use of this biological material is to implement strict quality control procedures to ensure that no samples are lost, and to quantify the exact amount of material needed for a given research programme.

If a pre-defined quantity of derivative products is supplied for a given research programme (rather than the whole sample in native form) it is possible to use the same sample for several research programmes.

Given this context, it is preferable to supply derivative products rather than whole samples.

Sample surplus may not be used for any other research programme than that originally defined. In the same way, the use of personal data is restricted to the original research programme (but may be further analysed if they are made totally anonymous).

6. Exporting samples outside of France

The only organisations that may import and export tissue and cells for research purposes are those authorised to do so by the Ministry of Research.

If the exported tumour samples are accompanied by informative medical data, these data must not be either directly or indirectly nominative. Otherwise, specific terms and conditions must be met (see article 5 of this charter).

7. Partnership with a foreign company

A partnership agreement may be signed between a French tumour bank management facility and a foreign company.

Contracts drawn up between a partner in France and a partner abroad may designate the legislation applicable to the foreign partner as being the legislation applicable to the contract. Nevertheless, the performance of such a contract in France must not, in any event whatsoever, contravene public order provisions in France.

Moreover, a company located abroad may wish to impose further obligations on its French partner. This may occur, for example, when a large corporation wishes to harmonise its international agreements.

These further obligations may be incorporated into the partnership agreement, further to case-by-case negotiations. However, national patient protection laws must be respected in all circumstances.

The very purpose of this charter is to inform research scientists on the rules that govern their activities. As long as they adhere to these rules, they will be protected with respect to any other demand made on them.

ARTICLE 5

Human tumour samples used for research purposes may be accompanied by directly or indirectly nominative data that is processed electronically. In this case, the necessary formalities must be completed with the national data protection authority (CNIL).

In the case of a joint research programme, the transfer of directly or indirectly nominative data shall comply with strict regulations.

OBSERVATIONS

This article is a summary of current legislation

The extent of legislation on personal medical data is significant and includes both laws of a general nature and laws specific to data processing in the medical research sector. Accordingly, the research project manager is advised to consult the CNIL representative within his or her organisation.

Generally speaking, human tumour samples can only be used for the benefit of the patient if they are accompanied by information relating to the patient's medical history. This information is usually stored in an **electronic data base**. Indeed, if a sample is subsequently to be put to effective use, it must be possible to determine its origin and to obtain **all necessary information on the patient and his or her condition**.

This information is private and personal and must be highly protected. Its disclosure is likely to affect the rights and liberties of the patients concerned.

In order to protect these rights and liberties, the data protection act of 6 January 1978, as amended on 6 August 2004, defines the rules to be observed when collecting data and storing and transferring **nominative information**.

If the research programme requires access to non-anonymised data:

1. **The files held by the tumour bank management facility** are separate from those containing the patient's medical records. The facility's top priority must be to ensure that the information in these files remains confidential.

A second priority is to make sure that patients are informed of the use of their personal data for research purposes, and that they are entitled to object to such use and to rectify the data. At the same time, patients may be given information on the use of tumour samples (this information is included in the document in appendix 1).

All necessary measures must be taken to protect nominative data and to prevent information covered by medical privilege from being disclosed or used for immoral purposes.

The CNIL recommends encrypting all medical data saved to a hard drive or any other back-up medium.

Other basic precautions must also be taken (protect access to the computer system, protect personal codes, run anti-virus software regularly, make sure that staff are aware of security measures, etc.). The CNIL guidelines contain useful information on these measures.

2. A number of **preliminary formalities** must be completed before such a file can be put together. More often than not, these formalities consist in submitting a notification to the CNIL.

Note, however, that these formalities may be reinforced according to the type of file in question. For example, the automatic processing of **genetic data** may, in some circumstances, require an application for authorisation rather than just a straightforward notification. (art. 25-2 of the act).

Please refer to the CNIL for information and advice (see address below):

Commission Nationale de l'Informatique et des Libertés
21, rue St Guillaume
75340 Paris cedex 07
France
Tel. +44 (0)1.53.73.22.22
Fax. +44 (0)1.53.73.22.00
<http://www.cnil.fr>

3. **Within the framework of a joint research programme, the transfer of directly or indirectly nominative medical data to a third party must comply with a number of formal rules.**

Data Protection Act no.78-17 of 6 January 1978 (as amended) allows health professionals to disclose personal medical data held for research purposes (such as epidemiological and observational studies, clinical trials and pharmacovigilance activities) under certain conditions only. These conditions are set forth in chapter 9 of the Act.

Two situations are possible:

- 1- The joint research programme uses anonymous data. These data may derive from another research project or from a treatment programme organised by the tumour bank management facility; they may also stem directly from the activities conducted within the framework of the joint programme itself.

The processing of such medical data is subject to prior notification to the CNIL and, in some cases, CNIL authorisation (cf. point 2 above).

The tumour bank management facility may transfer only totally "anonymised" data to its partner, so that the patient cannot be identified. This "anonymisation" is compulsory, in accordance with medical privilege laws (Art. L 1110-4 of the Public Health Code). Provided that data are completely anonymous, they can be transferred freely both within and outside the European Union.

- 2- The tumour bank management facility and its partner implement a joint research project requiring access to directly or indirectly nominative data. The partner actually conducting the research activities must obtain prior authorisation from the CNIL. The authorisation application must be preceded by a request for an opinion from the following organisation: the advisory committee for data processing in the medical research sector (for more information on submitting a request for an opinion or an authorisation application, please refer to the above-mentioned CNIL website).

Moreover, the CNIL has just adopted a reference methodology, MR 001 (see appendix 5). This document is also available on the CNIL's website: cnil.fr). Barring a few exceptions, it applies to all biomedical research, as defined in article L 1121-1 of the Public Health Code. If a research project falls within the scope of application of this methodology, the promoter is not required to complete the above-described formalities. In this case, the CNIL only requires a "statement of conformity" to the reference methodology. Furthermore, if the promoter has already submitted a statement of conformity on a previous occasion, he or she does not need to complete any formalities whatsoever. Indeed, the same statement of conformity is

applicable to all the research conducted by the promoter and is valid for an unlimited period of time.

Once CNIL authorisation has been obtained, or the research partner has submitted a statement of conformity, the tumour bank management facility may transfer data to its partner, in accordance with the reference methodology.

In all events, the patients included in the study must be informed individually of their rights beforehand, so that they can, if they wish, object to the transfer of their personal data.

4. In regard to international data transfers, with the exception of the cases mentioned above, it is forbidden to transfer directly or indirectly nominative data to any country that does not provide the same data protection guarantees as France.

Furthermore, in regard to the transfer of personal data to countries outside the European Union, the research manager must:

- make sure that the level of legal protection offered in the country where the data will be processed is at least as high as in France,
- or obtain the express consent of the person concerned.

Therefore the **transfer of directly or indirectly nominative data should be avoided** as far as possible within the context of joint research programmes. Preference should be given to the transfer of completely anonymised data, containing no information at all that could possibly be used to identify the patient.

Appendix 1

Patient information document and confirmation of the patient's lack of objection to the use of tumour samples for research purposes

This document is given to the patient, and a duplicate is kept in the patient's medical file. The patient is not required to sign it.

Dear Sir or Madam,

We have performed (*or we are going to perform*) a biopsy (surgical excision) of your lesion of the (*name of organ*).

This biopsy was (*is*) necessary to establish a diagnosis of the lesion and determine the best treatment for you.

Should we not use the entire sample, we will keep the remaining fragment.

Part of this fragment will be stored for possible subsequent use in your treatment. It will be stored in, under the responsibility of

Another part may, unless you object, be used for cancer research purposes, in accordance with confidentiality requirements. You may inform the department of your objection at any time.

Your constitutional genetic information will not be examined without your written consent.

Case (*department*) manager (name and capacity)

.....
.....

For official use only

Name of patient:

Information issued on:

Patient objection: yes no

Name of case/department manager:

Signature:

"The medical data associated with the sample shall be stored in an electronic file, allowing them to be automatically processed as part of a research project. You have the right to access, modify and oppose these data, in accordance with the law".

In accordance with the law (art.16-1 and 16-6 of the Civil Code), this sample may not become an object of commerce and may not give rise to financial compensation on your behalf. It may be used for joint research programmes involving one or more public or private sector organisations.

Appendix 2

Patient information document and confirmation of the patient's consent to the use of tumour samples for research purposes, including the examination of constitutional genetic information

This document must be signed by the patient. It is kept in the patient's medical file, and a copy of it is given to the patient.

Dear Sir or Madam,

We have performed (*or we are going to perform*) a biopsy (surgical excision) of your lesion of the (*name of organ*).

This biopsy was (*is*) necessary to establish a diagnosis of the lesion and determine the best treatment for you.

Should we not use the entire sample, we will keep the remaining fragment.

Part of this fragment will be stored for possible subsequent use in your treatment. It will be stored in, under the responsibility of

Another part may, unless you object, be used for medical research purposes, in accordance with confidentiality requirements. We are planning to conduct research into ... (*type of research*), **which will require an examination of your constitutional genetic information**. We need your consent for this research and you can give it simply by signing this document below.

This consent can be revoked at any time.

The case (*department*) manager (name and capacity)

.....
.....

Name of the patient:.....

Patient's signature

Date when this document was issued to the patient:.....

For official use only

Name of the case/department manager:

Signature:

"The medical data associated with the sample shall be stored in an electronic file, allowing them to be automatically processed as part of a research project. You have the right to access, modify and oppose these data, in accordance with the law".

In accordance with the law (art.16-1 and 16-6 of the Civil Code), this sample may not become an object of commerce and may not give rise to financial compensation on your behalf. It may be used for joint research programmes involving one or more public or private sector organisations.

Appendix 3

PARTNERSHIP AGREEMENT FRAMEWORK

3.1 – “Straightforward” partnership:

A “straightforward” partnership is governed by a biological material transfer agreement, which must include the items listed below. It should be noted that, in some cases, this type of contract may be governed by public law.

- ❖ **The contracting parties** (the Establishment that manages the tumour bank and the Beneficiary, i.e. the entity receiving the biological material): for each party, indicate the name of the legal entity, the legal status/form, the capital and trade register number (if appropriate), the address of the head office and the name(s) and position(s) of the signatories.

Note: check delegations of signing authority – for a public-sector organisation, the agreement may also have to be signed by the financial control body.

- ❖ **Purpose:** non-exclusive supply by the Establishment to the Beneficiary of biological material, for the purposes of research conducted by the Beneficiary.

Note: specify the objectives of the research programme.

- ❖ **Delivery of the biological material:** describe in detail the type of biological material delivered, the delivery date(s), the medium/container used, the method of transportation, traceability data, accessory information/data provided by the Establishment and the delivery receipt (MTA) to be signed by the Beneficiary.

Note: this article is necessary for traceability purposes, and also to specify the items that the Establishment will supply. It may refer the reader to an appendix for more detailed information. Specify whether a second delivery is possible in the event of accidental destruction and, if so, within what timeframe. Include an example of the delivery receipt in the appendixes.

- ❖ **Legal and statutory compliance:** specify that the biological material was obtained by the Establishment in accordance with the provisions in the Civil and Public Health Codes relative to tissue and cell collection and, in particular, that the patients concerned were informed accordingly and did not express any objections and/or gave their full consent. Specify also that the Data Protection Act of 6 January 1978 has been observed, and that the Establishment guarantees that all biological material is anonymous. Indicate that the Establishment is authorised to store collections of biological samples and to transfer such samples to a third party for research purposes, within the framework of the present partnership agreement.

- ❖ **Storage and preservation by the Beneficiary:** specify that the Beneficiary undertakes to store the biological material in accordance with applicable regulations, and will ensure traceability and compliance with hygiene, safety and environment protection regulations.

- ❖ **Use of the biological material by the Beneficiary:** the Beneficiary may freely use the biological material for research purposes, within the framework of the programme stipulated in this partnership agreement. Any other use is excluded. The Beneficiary may not sell the biological material. The Beneficiary shall use the biological material under its own exclusive responsibility.

- ❖ **Financial arrangements:** specify the preparation and delivery costs payable by the Beneficiary to the Establishment, including transportation costs in the event that transportation is organised and paid for by the Establishment. Specify the invoicing terms: name and address of the person to whom the Establishment must send its

invoice(s). Specify the payment terms: bank transfer, cheque, delivery address, term of payment.

Note: details of costs may be provided in an appendix. Indicate, in particular, the cost of a second delivery in the event of the loss or accidental destruction of the biological material.

- ❖ **Term:** specify the term of the agreement, as of the date of signature by the two parties.
- ❖ **Termination:** either party may terminate the agreement in the event of a serious breach by the other party, which is not rectified within ___ days of sending formal notice by registered letter with advice of delivery.
- ❖ **Consequences of completing the term or terminating the agreement:** once the agreement term is over, or if the agreement is terminated due to a breach by the Beneficiary, the Beneficiary shall stop using the biological material. Specify what will happen to any remaining surplus: disposal by the Beneficiary.
- ❖ **Jurisdiction – resolution of disputes:** indicate that the agreement is subject to French law, notwithstanding any jurisdiction dispute rules. Specify that the parties shall seek an out-of-court agreement before referring the case to a tribunal.

Note: if the agreement is drawn up with a foreign beneficiary, it is advisable to specify clearly that French law applies. Furthermore, in regard to the assignment of jurisdiction, it should be determined whether the agreement is subject to public and administrative jurisdiction law.

3.2 – Extensive partnership: an "extensive" partnership is governed by a collaboration agreement relating to a research programme headed by the Beneficiary (acting on its own or in cooperation with one or more third parties). The Establishment participates in research activities and/or contributes specific know-how. The transfer of biological material associated with this collaboration may be governed either by a material transfer agreement including the items listed above (attached to the partnership agreement) or by appropriate clauses inserted directly into the partnership agreement itself.

The main provisions of a collaboration agreement:

- ❖ **The contracting parties** (the Establishment that manages the tumour bank and the Beneficiary, i.e. the entity receiving the biological material): for each party, indicate the name of the legal entity, the legal status/form, the capital and trade register number (if appropriate), the address of the head office and the name(s) and position(s) of the signatories.

Note: check delegations of signing authority – for a public-sector organisation, the agreement may also have to be signed by the financial control body. Furthermore, the agreement may involve other partners, depending on the size of the research project.

- ❖ **Purpose of the collaboration:** joint research work and/or contribution of specific know-how to a research programme, the subject and content of which are to be defined (with a detailed description in the appendixes).
- ❖ **Stages of the collaboration:** specify the number and duration of these stages, the procedures for moving from one stage to the next (will this require the express agreement of the two parties or will it be automatic unless one of the two parties objects? If necessary, allow for the mutual termination of the collaboration at the end of each stage, depending on the results obtained (or in view of the lack of results).
- ❖ **Collaboration management and decision-making:** provide for the establishment of a monitoring committee. Define its role, the terms by which it will convene (at a frequency determined by the parties and at the specific request of one party), its operating mode

(specify which party will chair the meetings and will draw up the agenda for them, where the meetings will take place and the procedures for replacing/standing in for committee members), the terms and conditions governing decision-making (unanimity of attendees or of the two parties?) and the production of minutes (indicate which party will be responsible for drawing up these minutes and within what timeframe, and that the final version of these minutes will have contractual value).

❖ **The respective contributions of each party:**

- 1- Specify the preparation and delivery costs payable by the Beneficiary to the Establishment, including transportation costs in the event that transportation is organised and paid for by the Establishment.
- 2- Define what each party will contribute to the collaboration (research and/or specific know-how and funds), without forgetting to mention the biological material supplied by the Establishment. Indicate the scope and content of each party's background intellectual property in relation to the results of the collaboration. If necessary, provide for a license to use the background intellectual property of the other party for the purposes of the collaboration.

For the purposes of this agreement, the Establishment shall supply biological material to the Beneficiary in a non-exclusive manner. Define the conditions by which this material will be used within the framework of the research programme.

❖ **Property / exploitation of results:**

Specify the rules for assigning intellectual property rights on the results achieved, according to the contribution of each party.

Specify the rules for managing these intellectual property rights, in particular for filing and maintaining patents.

Define the terms by which these results will be exploited, and any procedures governing financial compensation and exclusive rights.

- ❖ **Publications/communication:** define the procedures for drawing up a joint publications/communication programme relating to the results achieved and, if appropriate, recognise the right of each party to refer to this programme in its own communiqués/lists of partners.

- ❖ **Confidentiality:** specify the scope and duration (beyond the term of the agreement) of each party's non-disclosure obligations regarding confidential information belonging to the other party; this confidentiality clause must cover, in particular, the background intellectual property of each party, the results of the collaboration and the contents of the agreement; it shall be applicable to all the subcontractors called in by either of the parties (specify the terms), for whom the parties shall remain fully responsible in all events.

- ❖ **Term:** specify the term of the agreement, as of the date of signature by the two parties (or, if appropriate, define a retroactive date. The exact details of the research schedule should preferably be provided in the appendixes). Specify the terms by which the agreement may be extended or renewed (tacit renewal or compulsory express request for extension/renewal by the parties).

- ❖ **Termination/consequences:** either party may terminate the agreement in advance, subject to a period of notice to be defined. This period of notice should be different depending on whether the termination results from a breach by either of the two parties or is just for the sake of convenience.

Specify what will happen to the results of the collaboration in the event of premature termination, and whether either party will have the right to continue the research alone, and/or in cooperation with another party: in this case, specify the terms by which the withdrawing party will pass on to the remaining party the know-how/intellectual property required for the continuation of the project (licence? transfer?). This applies, in

particular, to the supply of biological material by the Establishment, should the Beneficiary wish to pursue the research programme.

- ❖ **Jurisdiction – resolution of disputes:** indicate that the agreement is subject to French law, notwithstanding any jurisdiction dispute rules. Specify that the parties will seek an out-of-court agreement before referring the case to a tribunal.

Note: if the agreement is drawn up with a foreign beneficiary, it is advisable to specify that French law applies. Furthermore, in regard to the assignment of jurisdiction, it should be determined whether the agreement is subject to public and administrative jurisdiction law.

- ❖ **Legal and statutory compliance:** specify that the biological material was obtained by the Establishment in accordance with the provisions in the Civil and Public Health Codes relative to tissue and cell collection and, in particular, that the patients concerned were informed accordingly and did not express any objections and/or gave their full consent. Specify also that the Data Protection Act of 6 January 1978 has been observed, and that the Establishment guarantees the anonymity of patients. Indicate that the Establishment is authorised to store collections of biological samples and to transfer such samples to a third party for research purposes.
- ❖ **Storage and preservation by the Beneficiary:** specify that the Beneficiary undertakes to store the biological material in accordance with applicable regulations, and will ensure traceability and compliance with hygiene, safety and environment protection regulations.
- ❖ **Use of the biological material by the Beneficiary:** the Beneficiary may freely use the biological material for the purposes of the joint research programme and (if relevant) exploiting the results thereof. Any other use is excluded. The Beneficiary may not sell the biological material but may sub-concede its rights of use to a subcontractor or sublicensee, appointed by the Beneficiary to participate in the research programme or the exploitation of results. The Beneficiary shall use the biological material under its own exclusive responsibility.
- ❖ **Expiration/consequences:** when the agreement expires, or if it is terminated due to a breach by the Beneficiary, the Beneficiary shall stop using the biological material provided by the Establishment. Specify what will happen to any human material surplus remaining on expiration/termination of the agreement: disposal by the Beneficiary or return to the Establishment. Should the agreement be terminated for the sake of convenience, provide for the continuing use of the material by the Beneficiary if necessary.

Appendix 4

MATERIAL TRANSFER AGREEMENT (Appendix to the partnership agreement)

The material transfer agreement relates to the research project and is drawn up between the Recipient and the Sender (specify the references of the partnership agreement).

The delivery to the Recipient of biological material belonging to the Sender (as well as its derivatives and any related data), and the use of this material, derivatives and data, are subject to the following terms and conditions:

- 1- The biological material, the derivatives of the biological material and any related data:
 - a. shall remain the property of the Sender,
 - b. shall be used solely for the research purposes described in the collaboration agreement to the exclusion of any commercial use,
 - c. shall not be distributed or transferred to a third party without the prior written consent of the Sender,
 - d. shall be used solely in accordance with the laws and regulations applicable to this type of material and data,
 - e. shall be used only in the premises described in the collaboration agreement and by persons working for the Recipient in the said premises, under the direct responsibility of the Recipient.

- 2- The Sender and the Recipient shall mutually comply with the valuation, confidentiality and publishing clauses set forth in the partnership agreement.

Recipient	Name and address of the organisation	
	Name and capacity of the person in charge	
	Telephone, Fax, Email	
Sender	Name and address of the organisation	
	Name and capacity of the person in charge	
	Telephone, fax, Email	
Biological material	Type	
	Quantity	
	Delivery date	
	Container used	
	Method of transport	
	Traceability data	
	Information/data provided	

SENDER

Name of the coordinator

Signature

Date

RECIPIENT

Name of the coordinator

Signature

Date

Drawn up in two original copies.

Appendix 5

This is the legal text from the "CNIL", the French national commission which guarantees the protection of individual rights in the framework of the exploitation of computer-stored data.

The text refers to the ratification of a reference methodology for the treatment of personal data used in biomedical research.

Appendix 6: Composition of the INCa work group

Laurent Borella, INCa
Marc Dupont, DHOS, APHP
Jean Christophe Hébert, INSERM legal department
Anne Janin, St Louis Hospital
Véronique Dubernard, St Louis Hospital
Véronique Daurat, DRCD, APHP
Dominique Delaplace, DAJ-DP, APHP
Pauline Passelecq, DAJ-DP, APHP
Philippe Arhets, DRCD, APHP
Richard Lubin, INCa
Pierre Botreau Roussel, Ministry of Health
Isabelle Erny, Ministry of Health

Appendix 7: Composition of the INCa/LEEM work group

Laurent Borella, INCa
Anne-Priscille Vlasto, Leem
Pierre-Yves Arnoux, Leem
Sylvie Bourven Berniot, Bristol-Myers Squibb
Xavier Coron, Sanofi-Synthélabo (Sanofi Aventis)
Jacques de Varine Bohan, AstraZeneca
Blandine Fauran, Leem
Fabrice Herbin, Sanofi-Synthélabo (Sanofi Aventis)
Anne Janin, AP-HP
Catherine Lassale, Leem
Alain Pierre, Servier
Aude Richter, Roche
Claire Sibenaler, Leem
Patrice Siret, Leem Recherche
Bruno Vignon, Pierre Fabre
Valérie Waze-Naceur, GlaxoSmithKline Pharma

Appendix 8: Charter project revisers

Société Française d'Hématologie (*French Haematology Association*)
Société Française du Cancer (*French Cancer Association*)
Société Française de Pathologie (*French Pathology Association*)
Fédération Nationale de Cancérologie des Centres Hospitalo-Universitaires (*National Federation of University Hospital Cancer Centres*)
Fédération Nationale de Cancérologie des Centres Hospitaliers (*National Federation of Hospital Cancer Centres*)
Fédération Nationale des Centres de Lutte Contre le Cancer (*National Federation of Anti-Cancer Centres*)
Fédération de l'Hospitalisation Privée (*French Federation of Private Hospitalisation*)
Union Nationale Hospitalière Privée de Cancérologie (*National Union of Private Cancer Hospitals*)
Fédération Hospitalière de France (*French Hospital Federation*)
Ligue Nationale contre le Cancer (*French National Cancer League*)
Haute Autorité de Santé (*French National Health Authority*)
Société de lutte contre le cancer de l'enfant et de l'adolescent (*Association for the Prevention of Cancer in Children and Adolescents*)
Fédération des Etablissements Hospitaliers et d'Assistance Privés (*Federation of Hospitals and Private Assistance Institutions*)
Conseil national de l'ordre des médecins (*National Medical Board*)

Académie des sciences (*Academy of Sciences*)
Comité Consultatif National d'Ethique (*National Advisory Ethics Committee*)
Federation of European Cancer Societies
Council of Europe
Institut National de la Santé et de la Recherche Médicale (*National Institute of Health and Medical Research*)
Centre National de la Recherche Scientifique (*National Centre for Scientific Research*)
Union Nationale des Associations de Parents d'Enfants atteints de Cancer ou de Leucémie (*National Union of Associations of Parents of Children with Cancer or Leukaemia*)
Assistance Publique-Hôpitaux de Paris (*Public Assistance-Hospitals of Paris*)
Société Française de Biologie Clinique (*French Association of Clinical Pathology*)
Association Française de Chirurgie (*French Association of Surgery*)
Académie Nationale de Médecine (*National Academy of Medicine*)
Agence de Biomédecine (*Biomedical Agency*)
Ministère de la Recherche (*Ministry of Research*)
Commission Nationale Informatique et Liberté (*Data Protection Authority*)
Les entreprises du médicament (*National Union for the Pharmaceutical Industry*)
Cancéropôle Grand Ouest (*Cancer research hub – Western France*)
Cancéropôle Grand Sud Ouest (*Cancer research hub – South Western France*)
Cancéropôle Ile-de-France (*Cancer research hub – Paris region*)
Cancéropôle Grand Est (*Cancer research hub – Eastern France*)
Cancéropôle Nord ouest (*Cancer research hub – North Western France*)
Cancéropôle Provence-Alpes-Côte d'Azur (*Cancer research hub – South Eastern France*)
Cancéropôle Lyon-Auvergne-Rhône-Alpes (*Cancer research hub – Lyon-Auvergne-Rhône-Alpes*)

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LEGAL TEXTS

Legal and statutory provisions⁹

(Updated on 16 November 2005)

Contents

Sampling – General Principles (Public Health Code)

Secondary use of human organs, tissues and cells (Public Health Code)

Examination of genetic information (Civil Code and Public Health Code)

⁹ These provisions are set out in the chronological order in which they appear in the Guidelines

Respect of the Human Body – Non-commercialisation (Civil Code)
Informing minors (Public Health Code)
Notification or authorisation (Public Health Code)
Exportation and importation (Public Health Code)
Automatic data processing (Data Protection Act)

Sampling – General principles

Public Health Code (extracts)

Article L1211-2

The removal and collection of human body parts and products may not be performed without the prior consent of the donor. This consent may be revoked at any time. [...]

Article L1211-3

It is forbidden to publicise the donation of human body parts or products for the benefit of a specific person or for the benefit of a given establishment or organisation. However, this prohibition does not apply to promoting to the general public the donation of human body parts and products.

Such promotional activities shall be conducted under the joint responsibility of the Ministry of Health and the Ministry of Education.

Doctors shall ascertain whether patients aged between sixteen and twenty-five are familiar with consent procedures relating to the donation of organs for transplantation. If not, they shall deliver this information individually and as soon as possible.

Article L1211-4

No financial compensation, of any form whatsoever, shall be granted to persons donating human body parts or products.

The costs related to the removal or collection of such parts or products shall be borne entirely by the healthcare facility performing the removal or collection.

With regard to the application of the provisions in chapter II, subdivision IV, book I of the first part of this code, the removal of organs, tissues or cells from a living donor for therapeutic purposes shall be considered an act of treatment.

Article L1211-5

The donor may not be acquainted with the identity of the recipient and the recipient may not be acquainted with that of the donor. No information enabling the identification of either the donor or the recipient may be disclosed.

This principle of anonymity may only be waived in cases of therapeutic necessity.

Article L1241-1

Human body tissues, cells or products may only be removed or collected from a living donor for therapeutic or research purposes, for developing or testing medical devices used in in-vitro diagnosis, for inspecting the quality of clinical pathology analyses, or for the purposes of the technical appraisals and inspections performed by the French Agency for the Safety of Health Products on human body tissues, cells or products, in application of the 1st paragraph of article L. 5311-2. [...]

Secondary use of human organs, tissues and cells

Public Health Code (extracts)

Article L1211-2

[...] the use of human body parts or products for a medical or scientific purpose other than that for which they were removed or collected shall be possible, unless objected to by the person from whom these parts or products were taken, who was duly informed beforehand of this other purpose. If this person is a minor or an adult under guardianship, any objections must be raised by the persons holding parental authority or the guardian. The obligation to inform may be waived in the event the person concerned cannot be found or when one of the advisory ethics committees mentioned in article L. 1123-1, consulted

by the research manager, decides that it is not necessary. Nevertheless, this waiver shall not be permitted if the samples taken consist of germinal tissues or cells. In this case, should the interested person be deceased, it shall be prohibited to use the samples for any other purpose than that for which they were originally taken. [...]

Article L1235-2

Organs removed during surgery performed in the interests of the patient may be used for therapeutic or research purposes unless, after being informed of the purpose of such use, the patient expresses an objection.

Where the patient is a minor or an adult under guardianship, the subsequent use of surgically removed organs shall be subject to lack of objection from the holders of parental authority or the guardian, who must be duly informed of the purpose of this use. In the event of a refusal on the part of the minor or the adult under guardianship, the subsequent use of the organs shall be prohibited. [...]

Study of genetic information

Civil Code (extracts)

Article 16-10

A person's genetic information may only be examined for medical or research purposes.

The person's written express consent must be obtained beforehand, once he or she has been duly informed of the nature and purpose of the examination. The consent document shall mention the purpose of the examination. It may be revoked without reason at any time.

Article 16-11

Genetic fingerprinting may only be used to identify a person within the framework of inquiries or investigations pending judicial proceedings, for medical or research purposes or to identify a member of the military killed during an operation led by the armed forces or attached formations.

With regard to civilians, genetic fingerprinting may only be performed on the orders of a judge, with a view to either establishing or contesting a parent/child relationship or obtaining or withdrawing grants. The express consent of the person concerned must be obtained beforehand. Unless expressly agreed by the person while alive, genetic fingerprinting may not be performed post-mortem.

Where genetic fingerprinting is performed for medical or research purposes, the express consent of the person concerned must be obtained in writing beforehand, once this person has been duly informed of the nature and purpose of the examination. The consent document shall mention the purpose of the genetic fingerprinting procedure. It may be revoked without reason and at any time.

Article 16-12

The only persons authorised to perform genetic fingerprinting for identification purposes are those officially approved to do so, in accordance with terms and conditions established by Council of State decree. In the case of judicial proceedings, these persons must, in addition, be registered on a list of court experts.

Article 16-13

No-one shall be subjected to discrimination based on genetic characteristics.

Public Health Code (extracts)

Article L1131-1

The examination of a person's genetic information or the identification of a person by genetic fingerprinting shall be governed by the provisions in chapter III, subdivision I, book I of the Civil Code and by the provisions in the present subdivision, without prejudice to those laid down in subdivision II of this book.

Nevertheless, where it is impossible to obtain the consent of this person or, if necessary, to consult the trustworthy person mentioned in article L. 1111-6, the family or, failing this, a close relation, the examination or identification procedure may be undertaken for medical purposes, in the interests of the person concerned.

In the event of a serious genetic anomaly being diagnosed during the examination of a person's genetic information, the doctor shall inform the person or his/her legal representative of the health risks that would be incurred by potentially affected family members should he or she choose to remain silent, provided that preventive measures or treatment are possible. This information shall be written up in a signed document and given to the person concerned by the doctor. The person concerned shall then formally acknowledge receipt of this document. In this case, the doctor's obligation to inform the patient is fulfilled by the delivery of this document to the person concerned or to his or her legal representative.

The person concerned, or his/her legal representative, may choose to inform his/her family by the official procedure for transmitting medical information of a family nature. In this event, the person concerned shall give the doctor the names and addresses of his/her family members, and specify their relationship to him/her. The doctor shall then pass this information on to the Biomedical Agency, which in turn shall appoint a doctor to inform the said family members of the existence of family-related medical information likely to concern them, and how to access it. The procedures for collecting, transmitting, storing and accessing this information are set forth in a Council of State decree, issued after consultation with the Data Protection Agency.

Should a patient choose not to inform his/her family of the genetic anomaly, in accordance with the terms and conditions laid down in paragraph three, he/she shall not be liable to an action in tort.

Notwithstanding article L. 1111-7 and the second paragraph of article L. 1111-2, only the doctor who prescribed the examination of genetic information shall be authorised to give the results of this examination to the person concerned or, if necessary, the persons mentioned in the second paragraph of this article.

Article L1131-3

[...] All persons who, for research purposes, examine a person's genetic information or identify this person by means of genetic fingerprinting shall be authorised to do so in accordance with statutory terms and conditions.

Article L1131-4

The storage and processing of human body parts and products, including the collection and use of human biological samples for genetic research purposes, shall be governed by the provisions in articles L. 1243-3 and L. 1243-4.

Article R1131-1

The examination of a person's genetic information for medical purposes, in the sense of the present subdivision, serves to:

- either confirm or invalidate the diagnosis of a genetic disease in a person presenting the symptoms of this disease,
- or identify, in an asymptomatic person, the characteristics of one or more genes that are likely to lead to the development of a disease in this person or in his or her descendants.

Article R1131-15

The prescribing doctor shall keep the written consent document and the signed and commented copies of (i) the prescription for the genetic examination and (ii) the clinical pathology reports in the patient's medical file, in accordance with professional privilege.

The clinical pathology laboratories mentioned in article R. 1131-11 shall keep the clinical pathology reports and the related explanatory comments for a period of thirty years.

In all cases, these results shall be archived in secure and confidential conditions.

Please refer also to articles R1131-2, R1131-4, R1131-5 and R1131-14.

Respect of the Human Body – Non-Commercialisation

Civil Code

Article 16-1

Everyone has the right to respect for his/her body.

The human body is inviolable.

Neither the human body, nor its parts and products, may be the object of property rights.

Article 16-6

Persons permitting use of their bodies for experimentation or donating body parts or products shall not, under any circumstances, receive financial compensation for doing so.

Informing minors

Public Health Code (extract)

Article L.1111-2

(...)

The rights of the minors or adults under guardianship mentioned in this article shall be exercised by either the persons holding parental authority or the guardian. The latter shall receive the information provided for by this article, subject to the provisions in article L. 1111-5. The interested parties shall have the right to receive information themselves and to participate in any decisions concerning them, according to their level of maturity (in regard to minors) or their degree of discernment (in regard to adults under guardianship).

Notification or authorisation

Public Health Code (extract)

Article L1243-3

Any organisation that has notified the Ministry of Research beforehand may, for the purposes of its own research programmes, store and prepare human body tissues, cells, organs, blood, blood components and derivatives. These activities shall include the collection and use of human biological samples. Where this organisation is a healthcare facility, notification should be submitted to both the Ministry of Research and the locally competent Hospital Management Agency.

The term "collection of human biological samples" refers to the collection, for scientific purposes, of biological samples taken from a group of persons identified and selected according to the clinical or biological characteristics of one or more members of the group, and of the derivatives of these samples. The organisations mentioned in the first paragraph shall submit a notification for preliminary opinion to a specific committee, as defined in chapter III, subdivision II, book I of this section. The purpose of this committee shall be to evaluate the quality of information given to participants, the procedure for establishing consent and the ethical and scientific relevance of the project. The notification shall be addressed to the Ministry of Research and, if appropriate, the director of the locally competent Hospital Management Agency, at the same time as it is submitted to the specific committee. The latter shall issue an opinion without delay.

The Ministry of Research and, if appropriate, the director of the locally competent Hospital Management Agency may, within a legally-defined period of time, object to the proposed activities if the procedures for procuring, storing and using the human body tissues and cells do not adequately comply with the provisions laid down in subdivision I of this book, staff safety regulations or environment protection provisions. They may also object to these activities on the grounds of the quality of the information given to participants, the procedures for establishing consent and the ethical and scientific relevance of the project.

The Ministry of Research and, if appropriate, the director of the locally competent Hospital Management Agency may, at any time, suspend or prohibit any activities that no longer meet these requirements.

Prior to issuing a decision to object, suspend or prohibit, the Ministry of Research shall seek the opinion of the advisory committee for data processing in the medical research sector, provided for in article 40-2 of Data Protection Act no. 78-17 of 6 January 1978.

Notwithstanding the above paragraphs, the activities mentioned in paragraph one shall be governed by the provisions laid out in subdivision II, book I of this section when they are conducted within the

framework a biomedical research project, as defined in article L. 1121-1.

The French Agency for the Safety of Health Products shall be notified of any activities involving the storage or preparation of human tissues and cells for research purposes, that are conducted on the same site as similar activities for therapeutic purposes. In this case, the French Agency for the Safety of Health Products may request the suspension or prohibition of the notified activities for health safety reasons.

The organisations mentioned in the first paragraph may not transfer the human tissues or cells stored or prepared on their premises to another organisation, which has itself notified the authorities of similar activities.

Article L1243-4

Any organisation that stores or prepares human tissues or cells with a view to transferring them as part of a commercial activity for research purposes, including genetic research, must hold an authorisation issued by the Ministry of Research, further to a favourable opinion from the advisory committee for data processing in the medical research sector, provided for in article 40-2 of above-mentioned Act no. 78-17 of 6 January 1978.

The same authorisation must be obtained by any organisation that stores or prepares human body tissues and cells, with a view to supplying them free of charge for research purposes. Where this organisation is a healthcare facility, the authorisation shall be issued jointly by the Ministry of Research and the locally competent Hospital Management Agency.

The provisions of this article are also applicable to organisations that store and prepare organs, blood, blood components and blood derivatives.

Exportation and importation

Public Health Code

Article L1245-5

Without prejudice to the provisions laid down in article L. 1221-12 and the second paragraph of article L. 5124-13, the importation and exportation of human tissues, tissue derivatives and cells (whatever their level of preparation) and of cellular products for research purposes, shall be subject to authorisation. The only organisations entitled to perform these activities shall be those authorised to do so by the French Agency for the Safety of Health Products.

However, healthcare facilities authorised to collect haematopoietic cells from bone marrow for donation purposes, in application of article L. 1242-1, may export non-transformed bone marrow for therapeutic purposes. Healthcare facilities authorised to transplant bone marrow cells in application of article L. 1243-6 may import non-transformed bone marrow for therapeutic purposes.

Manufacturers of reagents, accessory therapeutic products and pharmaceutical products may import and export human tissues and cells intended, depending on the case, for use in the manufacture of reagents, accessory therapeutic products, proprietary medicines or industrially manufactured medicines.

The only individuals entitled to import or export biological samples shall be those whose activities include clinical pathology analyses, anatomo-cytopathology examinations, judicial appraisals or quality or assessment inspections (of reagents in particular).

The only organisations entitled to import or export tissues and cells for research purposes shall be those authorised to do so by the Ministry of Research.

Automatic Data Processing

Data Protection Act no. 78-17 of 6 January 1978, as amended by Act no. 2004-801 of 6 August 2004 (extracts)

Chapter IX: Processing data of a personal nature, for the purposes of medical research.

Article 53

The processing of data of a personal nature for the purposes of medical research shall be subject to the provisions in this Act, with the exception of articles 23 to 26, 32 and 38.

The processing of data relative to the individual therapeutic or medical follow-up of patients shall not be subject to the provisions in this chapter. The same shall apply to processing that enables the development of studies based on the data collected, if the studies are conducted by and for the exclusive use of follow-up staff.

Article 54

For each application for the processing of personal data, an advisory committee on the processing of data for medical research, established by the Ministry of Research and composed of competent persons as regards medical research, epidemiology, genetics and biostatistics, shall issue an opinion on the methodology of the research with respect to the provisions in this Act, the necessity of using personal data and their relevance to the purpose of the research, prior to submission to the Data Protection Authority.

The advisory committee shall issue its opinion to the applicant within one month. Failing this, the opinion shall be deemed positive. In the event of an emergency, this time limit may be reduced to fifteen days.

The chairman of the advisory committee may implement a simplified procedure.

A request for authorisation to process data shall then be submitted to the Data Protection Authority, which shall issue a decision in accordance with the terms and conditions laid down in article 25.

For the most common categories of automatic data processing in the medical research sector, involving data that does not allow the direct identification of the persons concerned, the Data Protection Authority may approve and publish standard methodologies, drawn up jointly with the advisory committee and public and private sector organisations, and designed to simplify the procedure outlined in the first four paragraphs of this article.

These methodologies shall specify, with respect to the characteristics mentioned in article 30, the standards to be met by data processing activities that are the subject of a simplified request for opinion and authorisation.

For processing that meets these standards, only a statement of conformity to one of these standards shall be sent to the authority. The chairman of the authority may approve this processing after a simplified examination procedure.

For other processing categories, the advisory committee and the data protection authority shall define the conditions in which an opinion is not required.

Article 55

Notwithstanding professional privilege regulations, healthcare professionals may release personal data as part of a data processing procedure authorised in accordance with article 53.

Where these data enable the identification of the data subject, they must be encrypted before transfer. However, this obligation may be waived in the event that data processing is associated with pharmacovigilance studies or research protocols conducted within the framework of national or international cooperative studies; this obligation may also be waived if the specific nature of the research requires it. The application for authorisation shall specify the scientific and technical grounds for the waiver and indicate the amount of time required to complete the research. At the end of this period of time, the data shall be stored and processed according to the terms and conditions set out in article 36.

In no event shall the data processing results be presented in such a way as to enable the direct or indirect identification of the persons concerned.

The data shall be released to the person in charge of the research project, who shall be appointed by the individual or legal entity authorised to perform data processing. This person shall ensure that requirements regarding data and processing security are met and that the specified purpose of the data processing is respected.

All persons either processing or having access to the data shall be bound to observe professional privilege, failing which the sanctions provided for in article 226-13 of the Criminal Code shall apply.

Article 56

All individuals are entitled to object to the waiving of professional privilege with respect to personal data concerning themselves, should this waiver be required by the type of data processing, as specified in article 53.

Should the research project require the collection of non-anonymous biological samples, the informed and express consent of the persons concerned must be obtained prior to data processing.

Data relating to deceased persons, including information on the death certificate, may be processed unless the interested party objected to such practice in writing during his or her lifetime.

Article 57

The individuals from whom personal information is obtained or whose personal data is transferred shall, prior to the processing of these data, be informed individually of:

1. The type of data transferred;
2. The purpose of processing these data;
3. The individuals or legal entities receiving these data;
4. The right to access and rectify these data, as provided for in articles 39 and 40;
5. The right to object to the use of these data, established in the first and third paragraphs of article 56 or, in the case referred to in the second paragraph of this article, the obligation to establish consent.

Nevertheless, it is possible to withhold this information in the event that, for legitimate reasons that the attending doctor has considered in good faith, the patient is not informed of a serious diagnosis or prognosis.

Where the data were originally collected for a purpose other than processing, the obligation of individual information may be waived when the persons concerned cannot be found. Any waivers of the obligation to inform individuals about the use of their personal information for research purposes must be mentioned in the authorisation application submitted to the Data Protection Authority, which shall rule on the matter.

Article 58

The information shall be delivered to holders of parental authority (for minors) or legal representatives (for adults under guardianship), who shall exercise the rights provided for in articles 56 and 57.

Article 59

Information relating to the provisions in this chapter must be provided in all establishments or centres where prevention, diagnosis and care activities entail the transfer of personal information for processing, as specified in article 53.

Article 60

The processing of data in breach of the terms and conditions in this chapter shall result in the temporary or permanent withdrawal, by the Data Protection Authority, of the authorisation issued in application of article 54.

The same shall apply in the event of a refusal to allow the verifications provided for in paragraph f, subdivision 2 of article 11.

Article 61

The transfer to a country outside the European Union of unencrypted personal data for processing and medical research purposes is authorised according to the terms and conditions set forth in article 54, subject to compliance with the rules laid down in chapter XII.

[...]

Chapitre XII: The transfer of personal information to countries outside the European Union.

Article 68

The data processing manager may only transfer personal information to a country outside the European Union if this country provides adequate protection of individual privacy, liberties and fundamental rights, with respect to the actual or potential processing of personal information.

The adequacy of the protection provided by the country shall be determined on the basis of the provisions in force in the country, the security measures implemented there, the specific characteristics of the data processing, such as its objectives and duration, and the type, origin and destination of the processed data.

Article 69

Nevertheless, the data processing manager may transfer personal information to a country that does not meet the requirements laid down in article 68, if the data subject has expressly consented to the transfer or if the transfer is necessary to meet one of the requirements below:

1. To save the data subject's life;
2. To protect the public interest;
3. To enable the establishment, exercise or defence of a legal claim;
4. To enable the lawful consultation of a public register which, in accordance with legal or statutory provisions, is intended for public information and is open to consultation by the public or by any person with a legitimate interest therein.
5. To fulfil a contract between the data processing manager and the data subject, or to implement pre-contractual measures defined at the request of the data subject;
6. To conclude or fulfil a contract, either drawn up or to be drawn up in the interests of the data subject between the data processing manager and a third party.

An exception may also be granted to the prohibition provided for in article 68, either by decision from the Data Protection Authority or, for the type of processing referred to in section I or II of article 26, by Council of State decree, issued further to the delivery of a reasoned opinion from the authority, where data processing procedures provide adequate protection of individual privacy, liberties and fundamental rights, due in particular to contractual clauses or internal rules governing data processing.

The Data Protection Authority shall inform the European Commission and the supervisory authorities in other European Union countries of any authorisations to transfer personal data, which it has decided to issue in accordance with the preceding paragraph. .

Article 70

If the European Commission has established that a country outside the European Union does not provide adequate protection in regard to personal data transfers or a category of personal data transfers, the Data Protection Authority, upon receipt of a notification filed in application of articles 23 or 24, mentioning that personal data will be transferred to this country, shall issue a receipt prohibiting the data transfer.

Where it deems that a country outside the European Union does not provide adequate protection in regard to personal data transfers or a category of personal data transfers, the Data Protection Authority shall immediately inform the European Commission. Where it has received a notification filed in application of articles 23 or 24, mentioning that personal data will be transferred to this country, the Data Protection Authority shall issue a receipt and may order the data processing manager to suspend the data transfer. If the European Commission establishes that the target country provides adequate data protection, the Data Protection Authority shall notify the data processing manager that the suspension has been lifted. If the European Commission establishes that the target country does not provide adequate data protection, the Data Protection Authority shall notify the data processing manager of the prohibition to proceed with the transfer of personal data to this country.