

# « *LeukoDB Charter* »

## Preamble

### ***Definitions:***

**LeukoTreat project:** means the European project funded by the European Commission under the 7th Framework Programme that aims at promoting the development of therapeutic strategies for the largest number of Leukodystrophy (LD) affected patients and further applications to more common white matter disorders. For this purpose, the project will combine the expertise of recognized European research teams, high technology enterprises, experts in medical ethics and LD patients and families associations devoted to LDs.

**LeukoTreat Ethics Committee:** means the independent committee which makes recommendations to the Steering Committee and General Assembly upon the issues addressed by the partners in the project and/or on the issues that the Ethics Committee will identify. It is also in charge of the dissemination of the identified best practices.

**LeukoDB:** means the LeukoTreat Project database.

**LeukoDB Committee:** is the committee in charge of the management of data, samples and mutations collected in WP1 and support per form of LDs in other RTD WPs.

**LeukoDB Network:** means the network in charge of documenting the LeukoDB. At the moment, it is composed of *LeukoRec France*, *LeukoRec Germany*, and *LeukoRec Italy*.

**Members and Partners of the *LeukoDB* Network:** entities listed in Annex which may be amended during the course of the LeukoTreat project.

**LeukoDB Charter:** means the present document which sets out the principles agreed upon by the Members of the LeukoDB Network, created in order to bring together data from identified LD patients.

**LeukoDB Coordinator:** means the person in charge of the *LeukoDB*.

**Participants:** means persons whose data is entered into the *LeukoDB*.

**Documenting Entity:** means the persons who are entering data into the *LeukoDB*.

### ***Technical aspects of the LeukoDB:***

The *LeukoDB* is located at Soluscience (France) partner of the LeukoDB Network. The LeukoDB uses the secured DB2 and is managed by IBM France. Technical aspects concerning security, anonymisation and protection of the data are detailed in Appendix (II) to the present Charter.

### ***Purpose of the LeukoDB Charter:***

- a. To ensure transparency of the *LeukoDB* functioning for the Members and Partners of the *LeukoDB* Network.
- b. To inform participants about the data used through the *LeukoDB*.
- c. To inform Members and Partners of the *LeukoDB* Network about their commitment regarding the LeukoDB functioning.

The *LeukoDB* Charter was validated by the *LeukoTreat Ethics Committee*. It is based on reference international texts concerning personal data protection and on recommendations from International Organizations. This Charter fully endorses the principles regarding personal protection data issued by the following:

*Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.*

*Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo). Council of Europe, Strasbourg, 4-04-1997.*

*Recommendation n° R 97 (5) on the Protection of Medical Data, Committee of Ministers, Council of Europe, 13 February 1997*

*Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, 25 January 2005.*

*International Declaration on Human Genetic Data, UNESCO, 16 October 2003*

*OECD Guidelines on the Protection of Privacy and Transborder Flows of Personal Data*

In accordance with the universal principles of Dignity and Primacy of the human being, as defined in Chapter one of the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Convention on Human Rights and Biomedicine, Council of Europe, Strasbourg, 4-04-1997),

*Article 1 – Purpose and object*

*Parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine.*

*Each Party shall take in its internal law the necessary measures to give effect to the provisions of this Convention.*

*Article 2 – Primacy of the human being*

*The interests and welfare of the human being shall prevail over the sole interest of society or science.*

and in accordance with article 6 of International Declaration on Human Genetic Data (UNESCO, 16 October 2003),

*Article 6 – Procedures*

*(a) It is ethically imperative that human genetic data and human proteomic data be collected, processed, used and stored on the basis of transparent and ethically acceptable procedures. States should endeavor to involve society at large in the decision-making process concerning broad policies for the collection, processing, use and storage of human genetic data and human proteomic data and the evaluation of their management, in particular in the case of population-based genetic studies. This decision-making process, which may benefit from international experience, should ensure the free expression of various viewpoints.*

*(b) Independent, multidisciplinary and pluralist ethics committees should be promoted and established at national, regional, local or institutional levels, in accordance with the provisions of Article 16 of the Universal Declaration on the Human Genome and Human Rights. Where appropriate, ethics committees at national level should be consulted with regard to the establishment of standards, regulations and guidelines for the collection, processing, use and storage of human genetic data, human proteomic data and biological samples. They should also be consulted concerning matters where there is no domestic law. Ethics committees at institutional or local levels should be consulted with regard to their application to specific research projects.*

by signing this Charter, Members and Partners of the *LeukoDB* Network further undertake to comply with the following recommendations:

## I/ Data processing

### a. *Data included in the LeukoDB*

(1) Data stored in the LeukoDB concerns patients suffering from Leukodystrophies and other genetic diseases affecting the brain white matter.

This data includes:

- pseudonymised sociodemographic data
- data extracted from patient's medical record, specially biological, radiological, electrophysiological data, genetic studies and cognitive evaluations.

(2) It will also include data from asymptomatic persons from patient's family.

### b. *Data Entry and data access issues in LeukoDB.*

(3) Members and Partners of the *LeukoDB* Network ensure that the access to data is restricted to scientific purposes. They respect principles contained in the information given to participants, his/her representative or his/her heirs.

According to this,

(4) Prior to documenting the LeukoDB, the Documenting Entity needs the following:

- 1) Permission from local data protection and ethics authorities (favourable opinion).
- 2) An agreement between the LeukoDB Coordinator and a documenting entity.
- 3) A password application form for each user of the database.
- 4) Signed informed Participant consent forms for each Participant containing the information listed in part 3 of the present charter.

(5) Regarding his/her own status – patient, general practitioner, clinician, researcher, clinical trial center – and the type of data – personal data, clinical data, biological data – an access right is determined for each user of the *LeukoDB*, as defined in the *LeukoTreat* project.

An access right to the *LeukoDB* can also be granted to further actors of the project. Members and partners ensure that this access will be granted in due consideration of the sensitivity of such data.

Access to data from the LeukoDB for projects not defined in the LeukoTreat Project is made through a specific request sent to the LeukoDB Committee. If the request is accepted, an agreement with (UDA, INSERM, UPD-P7, UKE, EKUT, IGG, OPBG and FIINCB) and with the Ethics Committee is necessary for the exploitation of these data and samples.

*c. Person and data protection issues*

(6) Members and Partners of the LeukoDB Network ensure that all Participants have a full access to their personal data, in compliance with the Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.

*(41) Whereas any person must be able to exercise the right of access to data relating to him which are being processed, in order to verify in particular the accuracy of the data and the lawfulness of the processing; whereas, for the same reasons, every data subject must also have the right to know the logic involved in the automatic processing of data concerning him, at least in the case of the automated decisions referred to in Article 15 (1); whereas this right must not adversely affect trade secrets or intellectual property and in particular the copyright protecting the software; whereas these considerations must not, however, result in the data subject being refused all information;*

(7) Members and Partners of the LeukoDB Network are fully conscious of the sensitivity of the data contained in the *LeukoDB* and commit themselves to take it into account through their activities, in accordance with the International Declaration on Human Genetic Data (UNESCO, 16 October 2003).

**Article 4 – Special status**

*(a) Human genetic data have a special status because:*

*(i) they can be predictive of genetic predispositions concerning individuals;*

*(ii) they may have a significant impact on the family, including offspring, extending over generations, and in some instances on the whole group to which the person concerned belongs;*

*(iii) they may contain information the significance of which is not necessarily known at the time of the collection of the biological samples;*

*(iv) they may have cultural significance for persons or groups.*

*(b) Due consideration should be given to the sensitivity of human genetic data and an appropriate level of protection for these data and biological samples should be established.*

According to this:

(8) Only participant data relevant to the LeukoTreat project is stored and processed. It is stored and processed without the Participant's personal data (name, address, social security number).

(9) The data that is processed is coded, which means that the data obtained from the *LeukoDB* is anonymous for researchers who analyse it, i.e. the identification of an individual Participant is not possible.

(10) Only the attending doctors can combine clinical data with personal data.

(11) Members and Partners of the LeukoDB Network ensure the confidentiality of the data, in accordance with the right to privacy of life, as defined by the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Convention on Human Rights and Biomedicine, Council of Europe, Strasbourg, 4-04-1997).

*Chapter III – Private life and right to information*

*Article 10 – Private life and right to information*

1. *Everyone has the right to respect for private life in relation to information about his or her health.*
2. *Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed.*
3. *In exceptional cases, restrictions may be placed by law on the exercise of the rights contained in paragraph 2 in the interests of the patient.*

According to this,

(12) The persons in charge of capture and validation of the data are bound by confidentiality rules, as defined in the Recommendation n° R 97 (5) on the Protection of Medical Data, Committee of Ministers, Council of Europe, 13 February 1997.

*3. Respect for privacy:*

*In principle, medical data should be collected and processed only by health-care professionals, or by individuals or bodies working on behalf of health-care professionals. Individuals or bodies working on behalf of health-care professionals who collect and process medical data should be subject to the same rules of confidentiality incumbent on health-care professionals, or to comparable rules of confidentiality.*

(13) Members and Partners of the LeukoDB Network ensure the anonymity of the *LeukoDB* data by the coding and securisation of it.

(14) Access to the *LeukoDB* shall be protected by password.

(15) No one except the Members and Partners of the LeukoDB Network and Participants themselves or their representatives and heirs will access to the *LeukoDB* data.

(16) Publication on the basis of the data will always be anonymous.

(17) Members and Partners of the LeukoDB Network ensure that each country in which data from *LeukoDB* is shared guarantees the same level of data protection and security, in accordance with the Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.

CHAPTER IV TRANSFER OF PERSONAL DATA TO THIRD COUNTRIES

Article 25

Principles

*1. The Member States shall provide that the transfer to a third country of personal data which are undergoing processing or are intended for processing after transfer may take place only if, without prejudice to compliance with the national provisions adopted pursuant to the other provisions of this Directive, the third country in question ensures an adequate level of protection.*

(18) Members and Partners of the LeukoDB Network ensure that *LeukoDB* data can never be used in order to stigmatize and/or discriminate the people concerned, in accordance with the International Declaration on Human Genetic Data (UNESCO, 16 October 2003).

**Article 7 – Non-discrimination and non-stigmatization**

*(a) Every effort should be made to ensure that human genetic data and human proteomic data are not used for purposes that discriminate in a way that is intended to infringe, or has the effect of infringing human rights, fundamental freedoms or human dignity of an individual or for purposes that lead to the stigmatization of an individual, a family, a group or communities.*

*(b) In this regard, appropriate attention should be paid to the findings of population-based genetic studies and behavioral genetic studies and their interpretations.*

(19) Members and Partners of the LeukoDB Network ensure the respect of the sensitive data; such data can only be shared for specific purposes, as defined in the Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.

*(33) Whereas data which are capable by their nature of infringing fundamental freedoms or privacy should not be processed unless the data subject gives his explicit consent; whereas, however, derogations from this prohibition must be explicitly provided for in respect of specific needs, in particular where the processing of these data is carried out for certain health-related purposes by persons subject to a legal obligation of professional secrecy or in the course of legitimate activities by certain associations or foundations the purpose of which is to permit the exercise of fundamental freedoms;*

(20) Members and Partners of the LeukoDB Network ensure that the participant have the right to withdraw his/her consent, as granted by the International Declaration on Human Genetic Data (UNESCO, 16 October 2003).

**Article 9 – Withdrawal of consent**

*(a) When human genetic data, human proteomic data or biological samples are collected for medical and scientific research purposes, consent may be withdrawn by the person concerned unless such data are irretrievably unlinked to an identifiable person. In accordance with the provisions of Article 6(d), withdrawal of consent should entail neither a disadvantage nor a penalty for the person concerned.*

*(b) When a person withdraws consent, the person's genetic data, proteomic data and biological samples should no longer be used unless they are irretrievably unlinked to the person concerned.*

*(c) If not irretrievably unlinked, the data and biological samples should be dealt with in accordance with the wishes of the person. If the person's wishes cannot be determined or are not feasible or are unsafe, the data and biological samples should either be irretrievably unlinked or destroyed.*

According to this,

(21) In case of withdrawal of consent, the data will be irretrievably unlinked so that it is no longer possible to identify the participant concerned.

(22) Withdrawal of consent can only be requested by the Participant him/herself. His/her wishes regarding his/her personal data shall be respected by any other person.

(23) For minors and incapable persons, the right to withdraw consent lies with the representative of the Participant.

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## II/ Regulation of potential value of data and valorization

Considering that data stored in the *LeukoDB* is issued from biological samples,

(24) Members and Partners of the *LeukoDB* Network ensure the respect of the principle of prohibition of financial gain and disposal of a part of human body, as defined in the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Convention on Human Rights and Biomedicine, Council of Europe, Strasbourg, 4-04-1997).

*Chapter VII – Prohibition of financial gain and disposal of a part of the human body*

*Article 21 – Prohibition of financial gain*

*The human body and its parts shall not, as such, give rise to financial gain.*

(25) Meanwhile, it is admitted that the data issued from the samples can be valorized in an economical way. In this context, such procedure shall be led in concert with all the actors of the *LeukoTreat* Project, Participants included.

(26) A subset of the data may be made available in the future to pharmaceutical companies. However, this will require a prior amendment of the present *LeukoDB* Charter as well as an express consent of the participant, his/her representative or heir, in compliance with the Additional Protocol to the Council of Europe Convention on Human Rights and Biomedicine, concerning Biomedical Research, 25 January 2005.

*CHAPTER IV – Information and consent*

*Article 13 – Information for research participants*

*vii. of any foreseen potential further uses, including commercial uses, of the research results, data or biological materials;*

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### III/ Participant information

(27) Members and Partners of the LeukoDB Network ensure the respect of the principle of autonomy of the human being, which is guaranteed by the respect of the information and consent procedure.

*Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, 25 January 2005.*

*CHAPTER IV – Information and consent*

*Article 13 – Information for research participants*

- 1. The persons being asked to participate in a research project shall be given adequate information in a comprehensible form. This information shall be documented.*
- 2. The information shall cover the purpose, the overall plan and the possible risks and benefits of the research project, and include the opinion of the ethics committee. Before being asked to consent to participate in a research project, the persons concerned shall be specifically informed, according to the nature and purpose of the research (...)*

According to this:

(28) Members and Partners of the LeukoDB Network ensure the respect of a « mutually enlightened » consent procedure: the Participant has obtained all the information he/she needs from a person in charge of the research. The Participant can reach a contact person for any further questions concerning his/her participation.

(29) Members and Partners of the LeukoDB Network ensure that data entered in the *LeukoDB* comes with a consent form which includes the use of data for research, properly signed by the Participant (or his/her representative) and the person in charge of the research, in compliance with the International Declaration on Human Genetic Data (UNESCO, 16 October 2003).

*Article 6*

*(d) It is ethically imperative that clear, balanced, adequate and appropriate information shall be provided to the person whose prior, free, informed and express consent is sought. Such information shall, alongside with providing other necessary details, specify the purpose for which human genetic data and human proteomic data are being derived from biological samples, and are used and stored. This information should indicate, if necessary, risks and consequences. This information should also indicate that the person concerned can withdraw his or her consent, without coercion, and this should entail neither a disadvantage nor a penalty for the person concerned*

(30) Members and Partners of the LeukoDB Network ensure that the Participant or his/her representative will be informed of the results of the research all along the project, as mentioned in the Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, 25 January 2005.

CHAPTER IV – Information and consent

Article 13 – Information for research participants

2. The information shall cover the purpose, the overall plan and the possible risks and benefits of the research project, and include the opinion of the ethics committee. Before being asked to consent to participate in a research project, the persons concerned shall be specifically informed, according to the nature and purpose of the research:

v. of arrangements for access to information relevant to the participant arising from the research and to its overall results

According to this,

(31) Participants involved in the *LeukoTreat* Project shall benefit from a priority access to the information concerning therapeutic protocols possibly issued from the research.

(32) Members and Partners of the LeukoDB Network are invited to keep a digitized consent form in the *LeukoDB*, signed by the Participant or his/her representative.

**(33) Concerning the entry of participant personal data in the LeukoBD, Members and Partners of the LeukoDB Network ensure that a consent form has been signed and that the Participant or his/her representative has received the following information:**

**A. Scientific Goal and information**

- Concerns data from Participants diagnosed with a leukodystrophy
- Mention of genetic research
- Data transfers between research teams
- Use of data for scientific research linked to leukodystrophies only

**B. Confidentiality**

- Transfer of data (between research teams, outside of the country) with the same degree of protection of the data everywhere.

**C. Access to the data**

- The data will be shared between the members and partners of the LeukoTreat project.
- The participant, his/her representative or heirs may access the data.

**D. Voluntary participation and freedom to withdraw the consent**

**E. Validation of the consent by an Ethics Committee**

(34) In addition, the LeukoTreat Ethics Committee recommends that the Members and Partners of the LeukoDB Network accept to inform the Participant, his or her representative or heir when they see them of the following:

**A. Scientific Goal and information**

- The data will be used in the LeukoTreat Project, including a description of the project
- Storage for an indefinite period of time in the LeukoDB
- Institution in charge of hosting the LeukoDB
- Indication of a contact person (name and address, email, telephone number)

**B. Confidentiality of data**

- Publication of only anonymous data
- Only Participant data relevant to the LeukoTreat project is stored and processed without the Participant's nominative data (name, address, social security number).
- The data that is processed is coded, which means that the data obtained from the LeukoDB is anonymous for researchers who analyse it, i.e. the identification of an individual Participant is not possible.

**C. Access to the data**

- No one except the Members and Partners of the LeukoDB Network and Participants themselves or their representatives and heirs will be granted access to the LeukoDB data.
- How the research results will be disseminated to the participants.
- Description of the procedure for the return of the results.

**D. Voluntary participation and freedom to withdraw the consent**

- In case of withdrawal, option to request irreversible anonymisation of the data already collected and stored.

**E. Validation of the consent by an Ethics Committee**

**F. Security of the data**

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**The Signatory has read and understood the present Charter, and commits itself to take fully into account its content.**

Date and signature:

N.B. This Charter might be further amended, with the accordance of the *LeukoTreat Ethics Committee*, depending on the demands to come in the *LeukoTreat* project.

## **Appendix I**

### Members and partners of the *LeukoDB* network:

**UNIVERSITE D'AUVERGNE CLERMONT FERRAND 1** France

**OSPEDALE PEDIATRICO BAMBINO GESU** Italy

**ISTITUTO GIANNINA GASLINI** Italy

**UNIVERSITAETSKLINIKUM BONN** Germany

**INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE** France

**SOLUSCIENCE SA** France

**THE UNIVERSITY OF MANCHESTER** UK

**FUNDACIO PRIVADA INSTITUT D'INVESTIGACIO BIOMEDICA DE BELLVITGE** Spain

**MAX PLANCK GESELLSCHAFT ZUR FOERDERUNG DER WISSENSCHAFTEN E.V.** Germany

**MEDIZINISCHE UNIVERSITAET WIEN** Austria

**TROPHOS SA** France

**UNIVERSITY COLLEGE LONDON** UK

**FONDAZIONE CENTRO SAN RAFFAELE DEL MONTE TABOR** Italy

**ACADEMISCH MEDISCH CENTRUM** Netherlands

**UNIVERSITE PARIS DESCARTES** France

**FRANCE EUROPE INNOVATION** France

**ASSOCIATION EUROPEENNE CONTRE LES LEUCODYSTROPHIES** France

**THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE** UK

**UNIVERSITE PARIS DIDEROT - PARIS 7** France

**FONDAZIONE IRCCS ISTITUTO NEUROLOGICO CARLO BESTA** Italy

**UNIVERSITAETSKLINIKUM HAMBURG-EPPENDORF** Germany

**EBERHARD KARLS UNIVERSITAET TUEBINGEN** Germany

**UNIVERSITY NEW SOUTH WALES** Australia

## Appendix II

### Security, anonymisation and protection of the data

LeukoDb is an "**Appliance**", i.e. a server providing the following features:

- A **database manager**, DB2 from IBM Company, to record all structured data.
- A **file manager** secured FTP server, to record all files like imaging, reports. The files are crypted before being recorded in the file server.
- An **application manager**, i.e. a system to provide installer for all used softwares on client computer. The main application is provided by Soluscience to handle pathology models in order to display all forms concerning it including lot of computing services. The system use "Open Office" to display publishing, "7-Zip" to compress and uncompress all documents when it is necessary, "dcm3d" library to display DICOM imaging. Some additional compounds like "R" to use advanced statistical tools can be provided too. An authorized user wishes to use this system will connect to a web link. After being authenticated, if the system is not already installed, the installer will start to import all the necessary applications.

Soluscience application uses DB2 to record all structured data in a secure way. Only this application can read and write information in this kind of database. This application can import and export data, but it's almost impossible to retrieve confidential information without this application. **User's authentication** depends on the the user's context.

- French user in health contex will use their "Health Professional Card" (CPS)
- Other user can use and id and a password
- Other user can also use a barcode.

The Soluscience application records data in the DB2 database locally and in the server. The application can work temporarily **without network** connection. Each time the connection is present the application tries to **synchronise** user's data in the client computer and the server.

### ***Right policy***

The **general admin** defines institution, a hospital, a research center... with a service list that can be used. This action will produce an object institution and a special user, called "**institution admin**". This admin can create new user, and can allocate them rights to use some services among the list he handles.

The system uses two different ways to set up the user's right

1. Each user has a **job profile**, ie the service list he has the right to use.
2. Each user has a list of important object he can use, like patient, medical protocol. The system will compute all object linked to this object list and will send to the user these informations.

So a user can only look for informations in his patient list with the service list he can use.

### *Data location*

The appliance will be installed during the first semester of 2011 in the **CHU of Clermont-Ferrand**. At the end of 2011, in accordance with the french law, the server will be installed in the **accredited center** of health data of IBM in France.

### *Service quality*

A **monitoring** of services will be installed to check regularly is the system works, and a **client support** will take place to collect issues (bug, conception) to redirect these information to the developer (Soluscience or IBM).