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neuGRID

A GRID-BASED e-INFRASTRUCTURE FOR DATA ARCHIVING/ COMMUNICATION AND COMPUTATIONALLY INTENSIVE APPLICATIONS IN THE MEDICAL SCIENCES

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RE	Restricted to a group specified by the consortium (including the Commission	
CO	Confidential, only for members of the consortium (including the Commission Services)	

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Executive summary

The present deliverable focuses on rules for commercial exploitation of clinical data and images.
In dealing with these rules, we argue from analogy with the rules related to commercial exploitation of biological materials. A revision of the European legal and ethical framework on commercial exploitation of biological materials has been performed, and a proposal of guidelines on the matter, that rests on the European normative framework, has been developed.
The suggested guideline covers three areas: 1. clinical data and images; 2. services and 3. research results and patent rights. The present guideline needs to be implemented by the competent bodies in the writing of final policies.

Rules for commercial exploitation of data

1. Introduction

The present deliverable focuses on rules for commercial exploitation of clinical data and images.
In dealing with these rules, we argue from analogy with the rules related to commercial exploitation of biological materials. The choice is due to the fact that the European documents and guidelines which form the legal and ethical European framework on commercial exploitation of clinical data focus in fact on exploitation of biological materials more than on exploitation of other kinds of clinical data.
We regard this analogy as a good one, in fact, even if clinical data and images are not part of the human body, they are nevertheless information coming from the study of the human body.
In dealing with the rules for commercial exploitation of clinical data and images we extend our discussion to the ethical aspects related to commercial exploitation of services connected to the use of data and to commercial exploitation of patents derived from the use of clinical data.
So our discussion will be on commercial exploitation of: 1. Clinical data and images; 2. Services connected to the use of data; 3. Research results and patents.
At the very beginning of our discussion, we need to point out that the NeuGRID consortium has a limited power of decision on the matter. In particular:

- with regard to point 1. Clinical data and images: clinical data and images that are going to be collected from subjects specifically enrolled to be entered in neuGRID project, will be collected within a clinical research project that is going to be promoted and coordinated by centers which are not exactly the same as the NeuGRID consortium. Moreover, this future clinical trial doesn't fall under the NeuGRID European Commission grant;
- with regard to point 2. Services and 3. Patents: the possibility of using services and patents as sources of financial gain will start, if ever, only at the end of the three years of the NeuGRID project, so the body that will deal with the matter will not be the actual NeuGRID consortium but a legal entity that does not exist yet.

Taking into consideration both the ethical importance of the clinical exploitation issues and the limited Consortium' power of decision on the matter, in the present deliverable we will propose guidelines which we strongly suggest to follow in the writing of the operative rules for commercial exploitation which the competent bodies will need to write and apply.

2. Methodological approach

A revision of the European legal and ethical framework on commercial exploitation of biological materials has been performed, and a proposal of guidelines on the matter, that rests on the European normative framework, has been developed.
A first draft of the proposal has been circulated within the partners of the NeuGRID Consortium for comments and suggestions, and a final proposal has been developed.
The final proposal will be submitted to the Independent Ethics Committee set up for the NeuGRID project and to the Ethics Committees of the partners.
Comments and suggestions from the Ethics Committees, if any, will be add to the present deliverable once the NeuGRID consortium will receive them.

3. Activity carried out and results

3.1 Revision of the European legal and ethical framework

The prohibition to commercialize the human body and its constituent parts is a principle acknowledged in the international legal framework.
In particular, with regard to the European situation, 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 (Oviedo, 1997), states that " The human body and its parts shall not, as such, give rise to financial gain" (Art. 21). Further, the Explanatory Report clarifies the meaning of the aforementioned provision affirming that: "...organs and tissues proper, including blood, should not be bought or sold or give rise to financial gain for the person from whom they have been removed or for a third party, whether an individual or a corporate entity such as, for example, a hospital".
In a similar way, the Recommendation of the Council of Europe on Research on Biological Materials of Human Origin, Rec(2006)4 15 March 2006, states that "Biological materials should not, as such, give rise to financial gain" (Art. 7).
On the basis of the principle that human biological material *per se* cannot be bought, sold or give rise to any profit, the donor cannot receive compensation for the donation of his/her tissues.
According to the Opinion of the European Group on Ethics in Science and New Technologies to the European Commission (July 1998, n.11) " All Member States of the European Union adhere to the principle that donations of human tissues must be free, following the example of blood, and this rules out any payment to the donor".
Similarly, Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells, among the principles governing tissue and cell donation, sets out that "Member States shall endeavour to ensure voluntary and unpaid donations of tissues and cells" (Article 12).
The recent Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products, at point 15 reaffirms once again the principle of altruistic donation, stating that "As regards the donation of human cells or tissues, principles such as the anonymity of both donor and recipient, altruism of the donor and solidarity between donor and recipient should be respected. As a matter of principle, human cells or tissues contained in advanced therapy medicinal products should be procured from voluntary and unpaid

donation. Member States should be urged to take all necessary steps to encourage a strong public and non-profit sector involvement in the procurement of human cells or tissues, as voluntary and unpaid cell and tissue donations may contribute to high safety standards for cells and tissues and therefore to the protection of human health".
The character of altruism of the donation has been the object of discussion in the literature, but the position in favour of the free and altruistic nature of donation, that need to be made in the spirit of generosity and solidarity, is clear in the European documents where the donation of biological materials is considered as a gift by the donor and it is forbidden to make profit from human biological material as such. In the Oviedo Convention Explanatory Report the prohibition of financial gain "does not prevent a person from whom an organ or tissue has been taken from receiving compensation which, while not constituting remuneration, compensates that person equitably for expenses incurred or loss of income (for example as a result of hospitalisation)"(Art. 21). Similarly, Directive 2004/23/EC, after affirming the unpaid donation, states that "Donors may receive compensation, which is strictly limited to making good the expenses and inconveniences related to the donation" (Article 12)

The prohibition to make profit from human biological material as such does not rule out the possibility of a gain as a result of legitimate scientific and technical services, nor the possibility of gain coming from patents which are the results of the use of the biological materials.
With regard to services, the Explanatory Report to the Oviedo Convention after affirming that biological materials should not be bought or sold or give rise to financial gain, states that "However, technical acts (sampling, testing, pasteurisation, fractionation, purification, storage, culture, transport, etc.) which are performed on the basis of these items may legitimately give rise to reasonable remuneration" (Art. 21, P.132). A payment from services is possible also under the CBDI Draft explanatory memorandum to the draft Recommendation on biological materials of human origin (Strasbourg 15 March 2006): "This provision [prohibition of financial gain] should not prevent payment for legitimate scientific or technical services rendered in connection with the use of such biological materials" and "In most cases, biothecnological products are developed from pooled samples and the contribution of any individual's sample is uncertain and unquantifiable" (Art. 7, P.35).
With regard to patentability, intellectual property rights arising from human biological materials donated for research may be sold or licensed.
The Explanatory Report to the Oviedo Convention clarifies that "The question of patents was not considered in connection with this provision [prohibition of financial gain] ; accordingly the latter was not intended to apply to the question of patentability of biotechnological inventions" (Art.21, P.134). The European Directive 98/44/EC on the legal protection of biotechnological inventions, after having clarified that the simple discovery of one of the elements of the human body cannot be patented, affirms that "An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element"(Art. 5). Also the European Directive 2004/23/EC on human tissue, though founded on the philosophy of voluntary and unpaid donation, altruism and solidarity between donor and recipient, limits its scope to non-manipulated, non- artificialized tissues, thus accepting the logic of donation for individuals and of economic reward for industry. Finally, the Regulation (EC) No 1394/2007 on Advanced therapy medicinal product and Tissue engineered product on the one hand affirms that "Where an advanced therapy medicinal product contains human cells or tissues, the donation, procurement and testing of those cells or tissues shall be made in accordance with Directive 2004/23/EC" (i.e. shall follow the principle of altruism and solidarity) (ART.3), and on the other hand set up the rules for Marketing authorization procedure for human tissue engineered products.

As it is evident, a distinction is made in the law between the "raw material" subjected to the rule of market inalienability, both for the donor and for the recipient, and the product (invention on this material) that may be source of profit through the patent law.
Moreover, the subject has no property right on this material: once the biological material is removed from the body and adequately anonymized, according to the legal framework, the material does not still belong to who it comes from. This principle has been strongly affirmed in a famous decision of the Supreme Court of California, the Moore case: in Moore v. the University of California [51 Cal. 3d 120 (1990)] the Court ruled that a donor does not have a "property right" in tissues removed form his/her body.
In conclusion, in the European regulation of property right related to biological materials there is an evident asymmetry between the fact that, on one hand, human subjects should give biological materials in the spirit of altruism and solidarity and, on the other hand, other people and bodies who use the subjects' biological materials can have a legitimate gain resulting from the use of those materials. That asymmetry deserve to be carefully considered and solved through ethical and legal instruments.

According to the legal framework, the subject has no propriety rights on his biological materials, but only the right to give informed consent both to the decision concerning his/her health and participation in research project, and to the commercial exploitation of the biological materials.
With regard to research, in the view of the Oviedo Convention the physician's right to store and use the biological materials for purposes other than intervention is balanced by the informed consent of the patient: "When in the course of an intervention any part of a human body is removed, it may be stored and used for a purpose other than for which it was removed, only if this is done in conformity with appropriate information and consent procedures" (Art. 22). In the Recc 2006(4) "Information and consent or authorization to obtain such materials should be as specific as possible with regard to any foreseen research uses and the choices available in that respect" (Art. 10) and, with regard to residual biological materials (Art. 12) "Biological materials removed for purposes other than storage for research should only be made available for research activities with appropriate consent or authorization, or in accordance with the provisions of art 22 paragraph 1-ii" [i.e. contacting the person is not possible with reasonable efforts and the research address an important scientific interest; the aim of the research cannot be reasonably achieved using biological materials for which consent can be obtained and there is no evidence that the person concerned has expressly opposed such research use].
With regard to the information about commercial exploitation of the biological materials, the CDBI Proposal for an instrument on the use of archived biological materials in biomedical research (Strasbourg, 17 October 2002) states that "In the context of a specific research project further relevant information may include [....] any foreseeable commercial uses of the materials and data, including the research results" (Art. 15.2). The Directive 98/44/CE, Preamble 26 affirms that "Whereas if an invention is based on biological material of human origin or if it uses such material, where a patent application is filed, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent thereto, in accordance with national law". Anyway, the amount of information due to the subjects, and the required specificity and explicitness of consent is a matter of discussion.

3.2 Proposal of guidelines for commercial exploitation of data

In absence of strict European regulation on the matter, the present proposal of rules for commercial exploitation of clinical data is the result of ethical considerations and discussions set up in the general European ethical and legal framework regarding commercial exploitation of biological materials. The guidelines are articulated in three parts: 1. Clinical data and images; 2. Services; 3. Research results and patent rights.

3.2.1 Commercial exploitation rules

3.2.1.1. Clinical data and images

Clinical data and images should not as such give rise to financial gain either to the subjects who take part in research projects, or to institutions collecting data, or to the consortium, or to a third party.
People should not receive any payment for their participation in the research protocol that should be regarded as a form of cooperation to the medical enterprise, and a sign of altruism and solidarity with the present and future patients. Both the data collection centres and peripheral researchers are forbidden to buy and sell the clinical data.
The prohibition of selling data should not prevent subjects from the possibility of reimbursement strictly limited to their expenses (i.e. expenses for travelling to the hospital for taking part in the research project). Any other kinds of compensation should not be foreseen (i.e. compensation for lost time and job).
The prohibition of buying and selling the clinical data and images as such does not rule out the possibility of a gain as a result of legitimate scientific and technical services or researches performed with the data.

3.2.1.2 Services

Even if for some extent the data de-identification procedure, the organization and uniformation of the clinical data which will be available from NeuGRID could be regarded as a service, no kind of payment should be foreseen for these operations, which are indeed the necessary conditions for the use of the clinical data for purposes of research. The distinction between selling the data and selling the services in case of a payment for these services would be in fact very slight.
It should be possible to foresee a fee for the access to neuGRID, at the end of the EC funding. The fee will be due not for the access to the clinical data and images, but for the access to the services of the Grid. The amount of the fee will be decided by the competent body that will be set up at the end of the NeuGRID project.
The main ethical criterium should be that, as far as it will be possible on the basis of financial needs, non-profit bodies will have priority, facilitated, or, whenever possible, free access to the infrastructure. This provision aims to guarantee the largest opportunities of research in a field, such as that of dementia, that deserves more research efforts.
The decision of the competent body regarding the access fee to the grid should be notified to an Independent ethics committee, as well as any changes in that policy.

3.2.1.3 Research results and patent right

The use of both the collected clinical data/images and the grid may give rise to research results that deserve to be patented (even though at present the consortium has not obvious reason to anticipate the development of patents in the near future). It will be possible to patent the research results and gain from the patent, according to the national, European and international patent laws.

In the case of a patent, the subjects who have taken part in the research project should not take part in the profit resulting from the patent.

Anyway, taking into consideration the abovementioned asymmetry between solidarity and altruism from the donor and possibility of a gain from other bodies which use the subjects' clinical data, the competent body that will be set up at the end of the three years NeuGRID project might consider a form of sharing benefits. In particular, a proportion of the gain from patents might be re-invested in research and development activities, whenever possible – based on partner's mission and local and historical circumstances – in the field of brain diseases.

3.2.2 Informed consent form

The rules defined for commercial exploitation of clinical data and images need be to be included in the information sheet of any subjects who will be enrolled in future studies that will be design to make use of neuGRID.
In particular, subjects should be informed that:
- no financial inducement is foreseen to take part in the research project and to "donate" clinical data for research purposes;
- no costs are charged to the participants in the research project;
- a reimbursement (if this is the case) is foreseen strictly limited to the subjects' expenses;
- the researchers, the hospitals and the sponsor of the research project are prohibited to buy, to sell or make profit from subjects' clinical data as such;
- the access to the clinical data and images is free, while a fee is due for the access to the grid (if this is the case); only profit bodies are charged with the fee (if this is the case);
- the use of both the collected clinical data/images and the grid for research purposes may give rise to research results that can be patented;
- the patent owner can obtain financial gain from the use of the patent;
- the research subjects will not get any financial benefits from the use of patent;
- the patent owner (if this is the case) is ready to share benefits, i.e. a proportion of the gain from patents will be re-invested in research and development activities, whenever possible, in the field of brain diseases (if this is the case).

Research participants have the right to refuse the participation in the research project and to withdraw their consent at any time, but they should be aware that if they give consent to take part in the research project, they actually consent also to the above commercial rules related to the use of their clinical data.
As well as the research protocol, the information sheet and informed consent form must be approved by the competent Independent Ethics Committees.

4. Conclusions

We have proposed an ethical guideline to control potential exploitation of clinical data and images.
The suggested guideline for commercial exploitation is set up in the ethical and legal European framework and covers three areas: clinical data/images; services and research results.
The present guideline needs to be implemented by the competent bodies in writing the final operative policies.