An update on the national general informed consent: what is the status quo of implementation at Swiss university hospitals?

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March 2020

Informed consent (IC) is an ethical and legal requirement for research involving human participants. From a research perspective, interest in using health-related data and samples from large patient populations has intensified. In response, different forms of IC have been proposed, with a preference for the so-called General Consent (GC), via which donors agree to the further use of their data and samples for potential research projects that have not yet

been defined. This article reviews: the legal basis of the GC in Switzerland; a short history about the process of reaching a harmonised GC at the national level; and the status quo of implementation in the five university hospitals in the country.

The general consent, what are we talking about?

In personalised medicine, the use of health-related data and samples from large patient populations have become an important resource for medical research (*Godard et al, Eur J Human Genet 2003, 11:88-122*). Many countries have established infrastructures for large biobanks and health registries. Among the best known are the UK Biobank, which recruited 500,000 individuals between 2006 and 2010; the Estonian Genome project; the International Agency for Research on Cancer Biobank ; and several US biobanks. One of the most important characteristics of such collections is that samples and data are gathered for long-term future use and not just for a single project (*Elger and Caplan, EMBO Reports 2006, 7:661-666*). These collections offer new opportunities for research, but the management of this data also raises new challenges, in particular regarding the management of the IC process.

According to the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), Good Clinical Practice (GCP) defines informed consent (IC) “a process by which a subject voluntarily confirms his willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject’s decision to participate. IC is documented by means of a written signed and dated IC form.”

It is clear that it is difficult, if not impossible, to obtain comprehensive IC for future research projects that are not yet specified, such as in the case of research conducted at prospective biobanks. This has led to the development of alternative IC approaches, including:

A *specific consent*, which requires donors to be recontacted for each future study;

B *tiered consent*, for which donors check the kinds of research for which their biospecimens may be used in the future;

C *dynamic consent*, which engages donors on an iterative basis;

D *blanket consent*, which involves no restrictions at all for future use of donated biospecimens; and

E *General Consent (GC)*, where donors can actively consent once for the current study and all future research involving the general use of their samples and information (*Master Z et al, Eur J Hum Genet 2015, 23:569-74*).

By far the most common model used today is the GC. It is considered acceptable and supported by several european countries, including Switzerland. However, GC should not be confused with open or blanket consent. Granting a GC means consenting to a framework for future research of certain types only. Key components of a GC include: the ethical review of each specific research project by an independent ethics committee, as well as the participants’ right to withdraw their consent at any time.

The legal basis of the GC in Switzerland: a complex and unique framework

In Switzerland, under certain conditions, the Human Research Act (HRA) and the Human Research

Ordinance (HRO), which came into force in 2014, allow the use of GC for further use of biological material and health-related personal data for research projects to be specified only in the future.

The law provides different rules, depending on the type of data (genetic or non-genetic) and on the possibility of establishing a link with the data subject and the biological material (anonymised, coded, or uncoded). Table 1 below provides a summary of these rules as set out in the HRA and HRO. As a basic principle, GC is sufficient for all research projects, except for those using uncoded biological material or uncoded genetic health-related personal data (HRA, art. 32, par. 2).

Further use of biological material and health-related personal data for research			Not informed or Active dissent	Informed without opposition	General Informed Consent	Specific Informed Consent
Non genetic health-related personal data (HRA, art. 33)	anonymised		✓	✓	✓	✓
	coded	(HRO, art.32)	x	✓	✓	✓
	uncoded	(HRO, art. 31)	x	x	✓	✓
Genetic health-related personal data (HRA, art. 32)	anonymised		x	✓	✓	✓
	coded	(HRO, art.29)	x	x	✓	✓
	uncoded	(HRO, art. 28)	x	x	x	✓
Biological material (HRA, art. 32)	anonymised		x	✓	✓	✓
	coded	(HRO, art.29)	x	x	✓	✓
	uncoded	(HRO, art. 28)	x	x	x	✓

Note: Cross = further use is not authorised; Check mark = further use is authorised. For a complete list of definitions, please refer to the insert next page. Table 1: Rules set out in the HRA and HRO, and the possibilities of using the GC

Definitions pertinent to interpreting GC

Biological material (HRA, art. 3, let. e) means bodily substances derived from living persons.

Health-related personal data (HRA, art. 3, let. f) means information concerning the health or disease of a specific or identifiable person, including genetic data.

Further use of biological material and health-related personal data (HRO, art. 24) is defined as any handling, for research purposes, of biological material already sampled or data already collected, and in particular:A procuring, bringing together or collecting biological material or health-related personal data;B registration or cataloguing of biological material or health-related personal data;C storage or inclusion in biobanks or databases;D making accessible or available or transferring biological material or health-related

personal data.

Anonymisation (HRO, art. 25): For the anonymisation of biological material and health-related personal data, all items which, when combined, would enable the data subject to be identified without disproportionate effort, must be irreversibly masked or deleted. In particular, the name, address, date of birth and unique identification numbers must be masked or deleted.

Coding (HRO, art. 26, par. 1): Biological material and health-related personal data are considered to be correctly coded in accordance with the HRA (art. 32 par. 2, and art. 33, par. 2) if, from the perspective of a person who lacks access to the key, they are to be characterised as anonymised.

Reaching a harmonised GC at the Swiss national level: a short history

The idea of reaching a GC for Switzerland began in 2006, when the Swiss Academy of Medical Sciences (SAMS) issued medical-ethical guidelines and recommendation for biobanks (*Biobanks: obtainment, preservation and utilization of human biological material. SAMS medical ethical guidelines and recommendation; 2006, withdrawn in Nov. 2013*). The SAMS guidelines stated that consent obtained from the donors of biological material "can generally also cover the further use of samples and data for future research projects". If research requires the removal of human biological material, envisages research with non-anonymized samples or poses risks, donors must expressly give their consent to a research project. Based on these guidelines, in 2010, a working group – consisting of the Swiss Biobanking Platform (SBP), the SAMS, and the data protection commissioner of the cantons of Zurich and Basel-Stadt – published templates for GC (information and consent) and for biobank regulations (*Salathé, Bulletin des médecins suisses 2010; 91:19-20*).

An update on the implementation of the Swiss GC

Since February 2019, hospitals and research institutions in other networks have now the opportunity to use a harmonised GC for their projects. The national GC covers the further use of coded genetic and non-genetic data and/or biological samples for research according to the HRO (arts. 29, and 32). The scope applies only to data and samples collected during the hospital stay and may include data from research projects. It does not cover additional data/sample collection (HRO, chap. 2), such as additional examinations or drawing additional blood samples. The national GC applies the *opt-in* option, meaning that the patients or their representatives must actively say *yes* to the use of their data/samples. Without this active *opt-in* option, the data and samples must not be used. The *opt-out* option – meaning that if no objection is communicated by the patient, but that patient was informed, the use of coded, non-genetic data or the anonymisation of samples is permitted – is not accepted within the national GC, even though it is allowed according to the HRA.

For adults lacking the capacity of judgement, their legal representatives will receive the same information as the patient. They are allowed to decide and sign on behalf of the patient. The same is true for children. Finally, in the case of incidental findings, donors are informed that they may be contacted if the findings are pertinent for their health and if a clinical action is possible. Donors who do not want to be informed at all about the existence of incidental findings must refuse GC.

Table 2 summarises the current state of use of the GC at Swiss university hospitals (this listing is based on direct communication between the SCTO Regulatory Affairs Platform and the respective institutions, from

December 2019 to January 2020). As of early 2020, two hospitals (Basel and Geneva) out of five are using the version 2 of the national GC, one (Bern) is also committed to implement it in 2020. Another hospital (Lausanne) is working on this version 2 to propose additional complements, as requested by their local ethics committee. A study is also planned in 2020 to test the different modalities of presentation of the GC to patients and to find out which model is preferred. The last hospital (Zurich) uses a local version of GC.

Overall, all the five university hospitals have had an established GC process in their institutions for a few years already, representing thousands of GC forms already signed by patients. As an example, at the University Hospital Geneva, the recruitment was launched on April 2017. Up to January 2020, around 40 000 patients signed the GC. Among them, 92% agree to the further use of their biological material and health-related personal data for research projects. These numbers prove the strong patients' engagement for research. They also illustrate how hospitals are efficient for recruiting in- and out-patients.

Table 2: The status quo of use of the GC at five Swiss university hospitals, as of January 2020

Institution	GC inception	Harmonised version (V2/2019) adopted?	Separate information for children?	Separate information for adults lacking capacity of judgement?	Extra sampling option	Incidental findings
University Hospital Basel	12.2015	Yes, since 12.2019	No. However, for children, the UKBB (University Children's Hospital Basel) uses its own GC.	No	YES, it is based on the GC, but it is regulated by a separate form for the respective research groups and approved by the EC.	Patients are informed in the case of incidental findings. If they do not want to be informed, they have to decline the GC.
University Hospital Bern	07.2014	Yes, implementation planned for 2020.	No	No	Yes. Additional information on a separate sheet.	Process still to be developed.
University Hospital Geneva	04.2017	Yes, since 09.2019.	(Yes). Separate information in development.	No	No	Patients are informed in the case of incidental findings. If they do not want to be informed, they must decline the GC
University Hospital Lausanne	11.2012	Harmonised GC will be implemented in April 2020, with some complements.	Topic to be discussed with EC-VD beginning of 2020.	Topic to be discussed with EC-VD, beginning of 2020.	Yes. Additional information about the Institutional Biobank and a second check box is included in the consent form.	Guidelines have been set up, in the case of incidental findings in the context of research project.
University Hospital Zurich	12.2015	GC corresponds to the harmonised GC except that unooded data are included according to Art. 31 HRO.	The children's hospital has its own version.	No. Specific procedures apply for patients in the intensive care units temporarily lacking capacity.	There is a template for additional sampling that can be adapted by the research team and that can be used in combination with the GC after approval of the ethics committee.	Decision of the treating physicians. In the case that patients don't want to be informed, they must decline the GC.

Complementary note: The Kantonsspital St.Gallen (KSSG) is using the same GC version as the University Hospital Zurich (since January 2019). They do not plan to use the harmonized version (V2/2019). The Ente Ospedaliero Cantonale (Bellinzona) planned to use the harmonized version. They will test the feasibility of the GC at the end of March 2020.

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Outlook

The adoption of a GC approach for the use of health-related data and samples represents an attempt to balance the needs of modern research to access large amount of data and samples with the matters of

privacy and security. Despite divergent opinions on certain aspects, the implementation of a national harmonised GC that guarantees access to and sharing of a large pool of biomedical personal data in accordance with the HRA, represents a significant milestone for research in Switzerland.

However, for the use of big data, the GC model must evolve, while respecting ethical, legal, and societal imperatives, towards a new, more interactive, transparent, and dynamic model, rather focused on the general public and not only on the patients. New consent solutions are currently under development throughout Switzerland and the article “Developing innovative procedures for obtaining informed consent: three solutions underway” gives an overview on some of them.

The announced revision of the federal ordinances on human research planned for the end of 2020 might also address this subject and provide more clarity. New topics around GC should be addressed too, such as the implementation of data governance structure to help the exchange of data.

Further Reading

1. Kegley J (2004) *Challenges to informed consent*. EMBO reports 5(9):832-836Caulfield T and Murdoch B (2017) *Genes, cells, and biobanks: Yes, there’s still a consent problem*. PLOS Biology 15(7): e2002654
2. Mikkelsen RB et al. (2019) *Brad consent for biobanks is best – provided it is also deep*. BMC Medical Ethics 20:71
3. Martani A et al. (2019) *Regulating the secondary use of data for research: arguments against genetic exceptionalism*. Frontiers in Genetics 10:1254