REGULATORY
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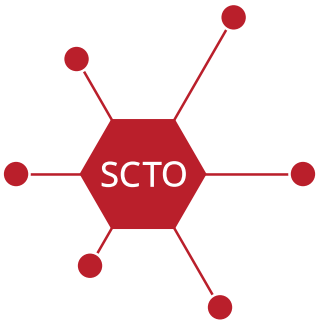

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Unique, credible, and regular updates on regulatory topics relating to human research

REGULATORY AFFAIRS WATCH

In this exceptional period we would like to thank and value the amazing work from our medical and research colleagues during these challenging times of the coronavirus pandemic. We are doing our best to ensure that we remain operational and continue to best serve the human research community.

Latest news to combat COVID-19

Sponsors, investigators and project leaders of clinical trials and research projects in Switzerland must ensure that the studies are conducted in line with the COVID-19 Ordinance 2 issued by the federal government on 16 March 2020 DE FR IT. Please visit the swissethics and Swissmedic specific webpages containing information on the conduct of clinical trials and research projects in Switzerland during the ongoing coronavirus pandemic:

- Joint guidance of Swissmedic and swissethics on the management of clinical trials with medicinal drug products (26 March 2020);
- Addendum to the patients information and consent form of clinical trials during the COVID 19 pandemic (26 March 2020);
- List of ongoing and submitted clinical trials and research projects on COVID-19.

On 20 March 2020, the European institutions published a guidance on how to manage clinical trials during the COVID-19 pandemic EN. The International Coalition of Medicines Regulatory Authorities reported pre-clinical data requirements and reminded the need to understand the theoretical risk that vaccines against COVID-19 enhance the disease prior to starting first-in-human clinical trials on 24 March 2020 EN.

IN THIS ISSUE

EDITORIAL: FASTEN YOUR SEATBELTS!

FASTEN YOUR SEATBELTS! WE HAVE SPEEDY TWISTS AND TURNS AHEAD

Take away from 2019

In April, we launched the RA Watch, intending to face the ever increasing activity and complexity of the regulatory aspects concerning human research in Switzerland – to track changes anticipated and offer them to you as a digest. Indeed, the legislation is undergoing continual development to stay abreast of and adapt to the many societal, technological, political fluctuations and ensure that Switzerland remains competitive.

We have not been disappointed! This timely matter has kept us fully engaged, observing and analysing events. In 2019, we saw the publication of a series of documents on the evaluation of the Human Research Act (HRA) and its ordinances, which entered into force in 2014; recommendations to adapt the law were published at the end of the year and should be implemented through coming months or years. Additional considerations – linked to the disruptive opportunities brought by new methods and technologies and the potential availability of ever more sharable data – have led to the elaboration of new documents. To mention a few, there are guiding principles and recommendations for registries in human research, the version 2 of the national General Consent (**GC**), key documents for biobanks, and more. A specific category of products, the medical devices, has also been scrutinised and draft ordinances were published and opened for consultation.

Perspectives for 2020

We're following many pertinent questions: How will human research be shaped in the year to come? How will Switzerland be affected, in concrete terms, by new European regulations, notably the EU General Data Protection Regulation EU 2016/679 (**GDPR**) and EU Clinical Trials Regulation EU 536/2014 (**CTR**)? How will the final legislation on medical devices look like?

Increased transparency (in particular, the publication of research results), open science, patient-centricity, larger numbers in patient recruitment, innovative trial designs, real-world clinical data and evidence, data governance, and the modernisation of institutional tools are all key themes that will keep regulators and the human research community on the edge of their seats this year. Let's start the year with an update on the GC.

Stay tuned with us. We'll keep you updated on all the trends, news, and twists and turns that this field will bring in 2020! Till then, take care of yourselves during this special time of coronavirus pandemic.

Séverine Méance, *RA Watch* Editor

COLLABORATING ON THE GENERAL CONSENT, THE KEY SUCCESS FACTOR

The use of health-related data and samples from large patient populations carries new promises for the development of novel therapeutic and diagnostic approaches for common and neglected diseases. However, prior to this use, written informed consent of patients who agree to the further use of their data and samples for potential research projects (so-called General Consent, **GC**) is required under the Swiss Human Research Act (**HRA**).

In the years following the enactment of the HRA in 2014, university hospitals faced several hurdles. First, paper-based GC processes revealed to be resource-intensive, leading to rather low GC coverage. Second, university hospitals developed individual GC versions with different contents, hindering the easy consolidation of data from different sources for nationwide analysis. Third, electronic approaches to GC through mobile devices was impeded due to the uncertain legal situation concerning electronic signature.

Thanks to the enormous efforts of different stakeholders, the situation has significantly improved over the last two years. Supported by the Clinical Trial Unit (**CTU**) network, swissethics, unimedsuisse and the Swiss Biobanking Platform (**SBP**), university hospitals teamed up to develop a national GC version, which is currently being implemented at the different sites. In addition, among other innovative projects, a nationwide electronic GC pilot project successfully passed the test of patient usability and is now ready to be developed into a validated application. Finally, the Federal Office of Public Health (**FOPH**) recently supported changes in the research ordinance required for the use of electronic signatures.

None of these recent developments would have been possible without a strong spirit of collaboration to make Switzerland an excellent place for high quality, innovative clinical research!

We hope you will enjoy reading the update provided in this RA Watch issue.

Christiane Pauli-Magnus,
President of the SCTO

NEWS FROM

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MANY STEPS MAKE UP THE MILE: TOWARDS A HARMONISED GENERAL CONSENT WITHIN SWITZERLAND

A journey of a thousand miles begins with a single step. This Chinese proverb comes to mind when one is considering the project of introducing a harmonised General Consent (GC) in Switzerland. Nobody knows where the journey will take us, but this much is certain – with the harmonised GC, adopted in 2019 by the university hospitals, the first step has been taken.

Introduction: taking the first step

The large amounts of data that hospitals produce daily represent a huge potential for medical research and innovation. Human Research in Switzerland 2018, a report on the research projects evaluated and approved by the Swiss ethics committees in 2018, shows that a significant portion of medical research today is made possible by the reuse of routinely collected data. A structured and transparent use of this data, taking into account the legitimate interests of protecting patients, is therefore an important contribution to medical progress.

Following the coming into force of the Human Research Act (HRA) in 2014, all five university hospitals have taken the opportunity to create a GC for the further use of data for research. Its introduction was taking place on a decentralised level, as the introduction in each institution was dependent on the approval of the respective ethics committee. This meant different solutions for the GC in the different university hospitals – whereby each of the implemented solutions was approved by the responsible ethics committee – and was therefore compliant to the HRA. After this initial and decentralised introductory phase, it was soon realised that national patient-centered research projects using health related data should be based on a harmonised consent solution.

Harmonising the different approaches of the various institutions and stakeholders involved is a complex undertaking. The major challenge lies in the fact that digitisation itself is a decentralised process that is inherently in constant conflict with the idea of centralised or harmonised solutions. This is all the more true as patients, hospitals, and researchers alike are constantly confronted with new possibilities, requirements, and risks stemming from the digital world.

A first milestone in the harmonisation efforts was reached in 2019: After intensive discussions, the version 2 of the GC template was published. The template was prepared by a working group of university hospitals and received a joint adoption by unimedsuisse, the Swiss Academy of Medical Sciences, and swissethics. It can be downloaded on the websites of unimedsuisse and swissethics.

The GC 2019 template finds the balance

When drafting the GC 2019 template, the focus was on making it conform legally with the HRA and be comprehensible to patients. In view of the complexity of the legal framework and terminology that is barely comprehensible to laypersons, a balance had to be found between describing legal details with precision and remaining understandable.

At the same time, the applicability had to be taken into account. For example, contacting a patient in the event of "incidental findings" – i.e. in the event of new findings or treatment options for them – can not be guaranteed, because in reality it is not always possible to locate former patients, years on. Yet, it is mentioned as an aim in the information. It is a question of honesty to make visible the practical limits and not to make false promises to patients.

The greatest benefit of the harmonised template lies in improving the protection of patient interests. This is achieved above all by the fact that with the GC 2019 template, the approval solution has become the standard. The contradictory approach, which is possible according to the HRA and has also been used in previous consensus solutions, has been abandoned. This contributes to the patients' understanding of the meaning of their individual decision and goes along with the EU General Data Protection Regulation (**GDPR**).

From a research perspective, the main advantage of the harmonised GC is that it simplifies research cooperation between different institutions and thus meets the current research settings in multicentre studies.

Last, but not least, the GC 2019 template will serve as a common basis for the further development of research infrastructures or innovative approaches for public participation in research. These include the projects of the Swiss Personalized Health Network (**SPHN**) with the development of IT interfaces, as well as electronic consent or – further in the future – the development of a dynamic consent system.

Developing governance as a core task

Currently, the harmonised GC 2019 template is being put into practice in university hospitals and several other institutions. This practical process is as important as the template itself. The implementation of appropriate governance in everyday hospital life is a complex undertaking that includes a wide variety of clinics, hospital-wide IT processes, and careful documentation. As a change process, it affects questions of corporate culture as well as the attitude of the individual researchers.

The unimedsuisse working group has addressed the common issues of implementation and has drawn up **a series of recommendations for applying the GC template**. They are available to be downloaded from the website of unimedsuisse. These explanations of how the GC 2019 template can be interpreted and applied are intended to facilitate its implementation. The recommendations explain, for example, what "no", "yes", and "no status" mean in concrete terms and how the patient data can be used according to the documented choices.

The recommendations pay specific attention to those patient groups in particular need of protection – namely children/adolescents and persons incapable of judgement. It provides a feasible approach to still include vulnerable patient groups for health related research projects considering actual hospital resources. If the process of consenting is designed appropriately, it is possible to apply the GC 2019 template to all these groups of patients. While some hospitals choose this solution, other hospitals differentiate the information provided, according to the patient's age.

The actual implementation, however, always remains the responsibility of the individual hospitals themselves. They must bear in mind that there is still no uniform practice among the regional ethics committees. To this end, it can be useful for hospitals to clarify their solutions individually with the ethics committee responsible for them.

Conclusion: Empowering the patient as the future challenge

The harmonised GC template represents an important step forward, setting a standard and allowing for convergence in practice. Following the adoption of the harmonised template, the focus at this stage is on its implementation in the hospitals. The recommendations that have been worked out among university hospitals should provide assistance in this regard. However, they do not relieve hospitals of the need to reflect on and shape governance within their institution. In a further stage, the experiences of implementation will have to be compiled and incorporated into further development of the GC.

But the development of the GC is not only a question of regulation and governance, forms, and procedures. It is embedded in the wider social and individual setting. The lay person as the general public are also on this journey of a thousand miles, as they are deeply affected by these issues. No matter how elaborate the consensus solution in hospitals, it cannot work out if patients cannot handle their own data and if they do not feel capable enough to make informed decisions. The development of the GC thus remains closely linked to the digital competencies and empowerment of the lay population. By developing public templates and procedures of the GC, university hospitals seek to contribute to this competence as well as to building trust in their institutions.

Susanne Driessen, President
swissethics, the umbrella organisation of the seven Swiss Ethics Committees on research involving humans

GENERAL CONSENT: SWISSETHICS' POINT OF VIEW

swissethics considers the concept of General Consent (**GC**) a highly useful tool for making patient data and samples available for research. An essential prerequisite for using GC agreements is that patients are informed in a fair and ethical manner with the GC form. Towards this statement, numerous technical options exist, depending on the type of data and encryption involved. Only after patients have received information that is both legally accurate and ethically conveyed, and have given their consent, their data and samples may be used in research.

Making data and samples available should provide long-term benefits to society – and potentially to the involved individuals as well – by allowing for the generation of knowledge per se and for the advancement of medicine and science as a whole. These benefits to the individual and society are both medically useful and desirable from an ethical standpoint.

However, every information document and consent form includes the dilemma: **how to convey information ethically and in an intelligible, concise and easy way, while at the same time ensuring its legal accuracy and completeness?** This dilemma is notoriously difficult to solve. To address this issue, swissethics and unimedsuisse elaborated version 2 of their GC template in February 2019. Since then, this template has been adopted by several university and non-university hospitals.

swissethics supports introducing a uniform, universally accepted national GC template. Its implementation would substantially contribute to the improvement of a number of key national research infrastructures such as the Swiss Personalized Health Network (**SPHN**) and the Swiss Biobanking Platform (**SBP**). Further efforts should therefore be made to implement a commonly accepted version of this document that balances comprehensibility with legal requirements.

swissethics has added short summaries in plain language which succinctly outline essential information at the beginning of many information sheets. Such a brief and visually appealing summary depicting the essential information for participants could be added at the beginning of the GC form as well. Also, in line with increasing technical possibilities, concrete plans need to be made for using e-consent and for relaying it via digital channels.

Introducing e-consent, including in the context of GC, requires amending legislation related to the Human Research Act (**HRA**) – a measure swissethics has long supported. Together, implementing such measures will determine whether and to what extent research participants are really involved in the research community in the future.

DEEP DIVE

AN UPDATE ON THE NATIONAL GENERAL INFORMED CONSENT: WHAT IS THE STATUS QUO OF IMPLEMENTATION AT SWISS UNIVERSITY HOSPITALS?

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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.

source CHUV 2017

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).

Table 1: Rules set out in the HRA and HRO, and the possibilities of using the GC

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)	✗	✓	✓	✓
	uncoded	(HRO, art. 31)	✗	✗	✓	✓
Genetic health-related personal data (HRA, art. 32)	anonymised		✗	✓	✓	✓
	coded	(HRO, art.29)	✗	✗	✓	✓
	uncoded	(HRO, art. 28)	✗	✗	✗	✓
Biological material (HRA, art. 32)	anonymised		✗	✓	✓	✓
	coded	(HRO, art.29)	✗	✗	✓	✓
	uncoded	(HRO, art. 28)	✗	✗	✗	✓

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.

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*).

Since the entry into force of the HRA in 2014 incorporating the concept of GC, the SAMS biobanks guidelines have been withdrawn. Then, swissethics, the SAMS, and unimedsuisse attempted to elaborate a harmonised Swiss-wide GC form that would take into account the regulatory requirements for the further use of health-related data and biological material. A first version of GC was published in 2017 SAMS, 2017 Model of General Consent.

However, patient organisations, hospitals, and representatives from the research community criticised this first version of the Swiss GC. They denounced its lack of clarity, in the terms and formulations used, and declared this first version too complex for participants to understand (*Evaluation report V1/2017 national consent; 2018*). In this context, in 2018, the five university hospitals together with unimedsuisse developed a second proposal for a harmonised GC (V2/2019). This new version took into account the comments and remarks raised previously, particularly, i) the issue of non-opposition that was one of the most debated issues; ii) the inclusion of additional blood sampling; iii) the GC for minors and adults lacking capacity of judgement; and iv) the return of results (incidental findings). This second version, adopted by the five university hospitals in September 2018 was then approved by the swissethics steering committee in November 2018. The document is available online in English, French, German and Italian from the websites of swissethics, the SAMS, and unimedsuisse.

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 on 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 uncoded 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.

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):832-836

2 Caulfield T and Murdoch B (2017) Genes, cells, and biobanks: Yes, there's still a consent problem. PLOS Biology 15(7): e2002654

3 Mikkelsen RB et al. (2019) Brad consent for biobanks is best – provided it is also deep. BMC Medical Ethics 20:71

4 Martani A et al. (2019) Regulating the secondary use of data for research: arguments against genetic exceptionalism. Frontiers in Genetics 10:1254

CONSIDERATIONS ON GENERAL CONSENT IN PAEDIATRICS

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The general goal of the initiative launched by the Swiss Personalized Health Network (**SPHN**) is to establish the infrastructure needed to collect and provide data and samples from Swiss residents, to ultimately support personalised approaches to healthcare.

For the paediatric population, the project "Harmonizing health-related data and biospecimens across paediatric hospitals" was set up to create a common database of health-related variables to be collected from inpatient children in Switzerland, and to develop a consensus among all major paediatric hospitals on which data and which samples should be stored. Through this project, a unified data structure and list of target samples, which could support future high-quality research projects in paediatrics, will be generated. General consent (**GC**) in paediatrics would allow for this data to then be available for research.

In 2018, a working group – consisting of paediatricians, adolescent physicians, a patient advocate and health lawyer, and a representative from the group of HIV-positive adolescents – was convened by the Swiss Academy of Medical Science (**SAMS**). This group created a fact sheet and a checklist on the topic of what to consider when seeking GC for research in the paediatric population. In January 2019, both documents were shared with and reviewed by **SwissPedNet** (Swiss Research Network of Clinical Pediatric Hubs) members, representing paediatricians conducting clinical research in Switzerland.

Under what circumstances is obtaining GC in paediatrics permitted?

GC aims to support the use of routine data and samples that are gathered as part of regular medical care for research. According to the Human Research Act (HRA), art. 22ff, research projects requiring data and/or samples from patients should be of potential benefit to the participating population. This, however, is rarely the case for children and adolescents as diseases are rare and long-term benefits often unclear.

However, importantly, the paediatric population should not as a result be excluded from research. Without data and samples from children, research projects cannot be conducted in this age group, and results obtained from research on adults, in general, cannot be extrapolated for children. The use of routine data and samples from this vulnerable group in fact serves to minimise the burden of research on them, by reducing their need to undergo additional visits and unpleasant interventions, while still potentially informing better approaches to future medical care. Therefore, processes and strategies should be implemented to obtain GC in children and adolescents.

What kind of written information is required for the paediatric population?

From a legal perspective, written information from the legal representative of a patient is central to the consent process, including for children and adolescents. As such, when children are younger than 14, their parents (or their legal representative) can decide on their behalf, taking into account the interests of the child, based on their knowledge and beliefs. It is, however, recommended that children and adolescents be "age-appropriately" informed about the study and give their assent verbally. If the patient is 14 years or older, both the adolescent patient and their parents are expected to indicate their consent in writing.

For many studies, this written information – which can be offered in as many as three to four types of format suited to the different types of addressee – is considered necessary:

1. The first, addressing the parent or legal guardian of children and adolescents: This version usually is similar to patient information for adults, but its greeting and wording are adapted, e.g. "your child is being approached to participate in…".
2. The second, addressing adolescents between 14 and 18: the content of this version corresponds to the patient information for adults, but the greeting is adapted, e.g. in German, French, or Italian, the address will be informal (using "Du" or "tu"). If appropriate, the unchanged written information prepared for adults can be given to youth aged 16 and older.
3. The third, addressing children of 11 to 13: In this version, the language is deliberately simplified, shorter, avoiding complex scientific or medical terms, and the facts are explained according to the patient's age. In addition, visual representations can be used.
4. Sometimes, depending on the study, a fourth type of written information is created to address children younger than 11. This form is typically very short (less than a page), relies as much as possible on drawings, and uses simple words to explain the study.

Double consent, always together with parent or guardian

According to the HRA (art. 23), teenagers older than 14 have the right to decide for themselves whether they wish to participate in a study that poses minimal risks. GC processes could be interpreted as being of minimal risk, as the patient's data are already available in the electronic patient record and their biosamples are "leftover" material. Nevertheless, the working group recommends double consent for youth of this age, meaning that the parents (or legal guardians) should be included in the GC.

The working group's reasoning is that the long-term effect of the use of these data and samples, progress in medical diagnostics, and the possibility that personally relevant findings may be generated in the future may affect the decision, and these eventualities cannot be fully evaluated by teenagers. Of course, when the teenager reaches legal adulthood at 18, they can independently reconsider and potentially withdraw their previously granted approval.

Recommending temporary consent

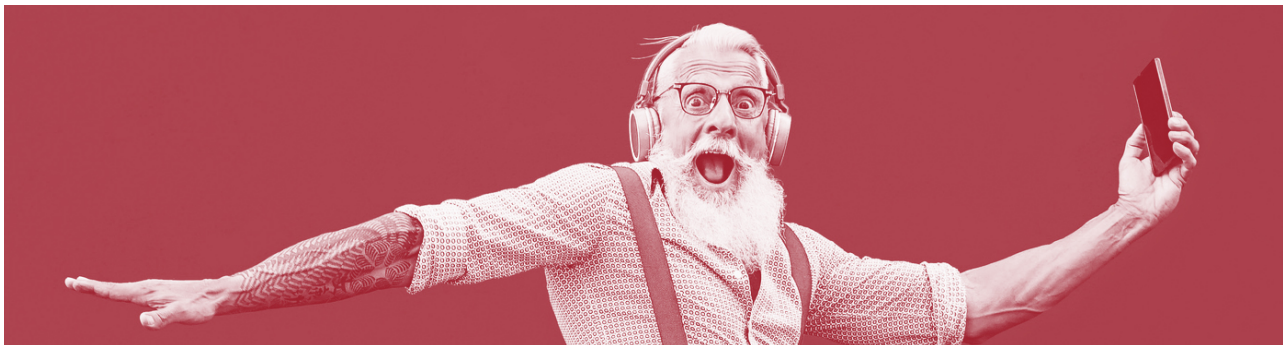
Intensive discussions took place about the issue of re-consenting children and adolescents when they reach adulthood. The working group decided that a GC should only be valid until the donor of data and samples reaches adulthood, i.e. until their 18th birthday. Nevertheless, technical hurdles hinder implementation of this recommendation and may substantially delay the use of longitudinal data for the paediatric population.

Over the years, the attitude towards the use of data and samples may change, as may the related research opportunities and their impact on society. From this perspective, using data and samples from a neonate or child for an unspecified period of time may be problematic. This topic remains pertinent and should be reviewed periodically.

Conclusion

The paediatric community is ready to implement a GC process within children's hospitals, countrywide. Although all SwissPedNet member institutions started with different information and consent forms, SwissPedNet decided to initiate a harmonisation process based on the template for adults, version 2/2019, issued by unimedsuisse.

The problem related to the transition to adulthood and to the transition from dual to single consent remains and needs to be revisited in the future.



DEVELOPING INNOVATIVE PROCEDURES FOR OBTAINING INFORMED CONSENT: THREE SOLUTIONS UNDERWAY

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The Swiss Personalized Health Network (**SPHN**), a national initiative funded by the State Secretariat for Education, Research and Innovation (**SERI**), was designed to promote the development of personalised medicine and personalised health in Switzerland. The SPHN aims to develop infrastructure projects that will make health-related data interoperable and shareable at the national level. Accordingly, certain projects related to informed consent (**IC**) were funded and are described in this article: the Electronic General Consent (**e-GC**), the Citizen Centered Consent: Shared, Transparent and Dynamic (the so-called **C3-STuDY**), and the proactive management tool of consent for research (in French so-called "Gestion Proactive des Consentements de Recherche", **GPCR**).

In the current, rising era of biomedical research that increasingly wants to access and use big data, the conditions for acquiring consent to research from patients must evolve in accordance with ethical, legal, and societal imperatives.

Many stakeholders are involved in implementing various principles, laws, rules, techniques, and procedures to cope with such a rapidly evolving environment. In order to meet these imperative requirements and to be practically able to manage massive access to sensitive health-related data, we need suitable technical innovations and validated solutions. Among those stakeholders involved is the Swiss Personalized Health Network (**SPHN**), a national initiative funded by the State Secretariat for Education, Research and Innovation (**SERI**) that was designed to promote the development of personalised medicine and personalised health in Switzerland. The SPHN aims to develop infrastructure projects that will make health-related data interoperable and shareable, at the national level. Accordingly, certain projects related to informed consent (**IC**) were funded and are described in this article: the Electronic General Consent (e-GC) and the C3-STuDY Citizen Centered Consent (referred to as C3-STuDY). Additionally, a third, also new consent management tool, rounds off this article: Gestion Proactive des Consentements de Recherche (**GPCR**, meaning proactive management of consent for research).

e-GC: a nationwide, harmonised, interactive tool

According to the Swiss Human Research Act (**HRA**) and its ordinance (Human Research Ordinance, **HRO**), further use of biological material and health-related personal data for research purposes requires the consent of patients. So far, as of 2017, a paper-based GC process with a handwritten signature has been established at all five Swiss university hospitals. Presenting paper consent forms to patients, however, calls for considerable resources: printing, explaining to patients, collecting, and transferring the consent forms into the electronic health record system.

Therefore, if more effort went into creating an easier distribution of the GC, such as by facilitating patient access to the consent form, the GC patient pool would be likely to increase and more research initiatives in personalised health would be likely to succeed.

The goal of the e-GC project is to extend the GC process by offering patients a flexible, patient-centric, and admission-independent electronic consent pathway. All five Swiss university hospitals agreed in late 2019 to participate in the testing of an electronic consent pathway at their institution.

Based on the national GC template (V2/2019), a user-interface prototype for the collection of the GC was developed by the Department of Clinical Research, University of Basel (mid-2018). The prototype was evaluated in different settings at the five Swiss university hospitals. Two options of giving consent were explored: using 1) patients' mobile phones, without any involvement of hospital personnel; and 2) a hospital device (a tablet) requiring explicit confirmation of patient identity by hospital personnel. Issues were documented by respective recruiters in each hospital and feedback from patients was collected through a survey, directly after the usability testing. The evaluation of the usability testing is ongoing and results should be released in the course of the year 2020.

C3-STuDY: shared, transparent, and dynamic exchange

The C3-STuDY project proposes moving towards a new model of consent for research, applying a more interactive, transparent, and dynamic approach, focused on the citizen rather than the patient. This revised approach promotes a proactive exchange of information between data providers and users. It aims to strengthen the transparency and traceability of all these processes, for which the responsibility should be better shared between citizens and researchers.

The project, based on innovative communication channels, might guarantee this two-way exchange of information. Better informed, citizens can make more independent choices, follow the evolution of the research in which they participate, change their preferences over time, and feel more engaged in such consent processes. As for researchers, they will be able to document their research in a more dynamic and transparent manner. This transparent and continuous exchange of information serves to strengthen the informational and societal value of research; it involves a change of role from a passive research subject to an active, interested, and valued participant.

This generic, transparent, dynamic, non-retractable but revocable and traceable consent management system was developed at the Hôpitaux Universitaires Genève (**HUG**) and uses a computer protocol called smart contracts. Thanks to a web tool or an App, citizens will be able to accept or refuse consent, and even revoke consent previously granted. The system will also allow researchers to find those participants who have already agreed to have their data used for research projects. The web interface and the Apps allow them at any time to consult the status of their consent and the recruitment rate of their studies or to launch information campaigns to call out and recruit participants.

A first version of the C3-STuDY tool was made functional in March 2019. As of early 2020, it was being tested for technical and security aspects, and discussions have started among certain university hospitals to clarify the architectural and technical constraints, envisaging production to start later in the course of the year 2020.

GPCR: a new consent management tool underway

Because legal and ethical requirements concerning data and sample reuse are very strict, university hospitals face some issues concerning research projects and data protection. Challenges include:

- How can personal data be disassociated from samples, yet remain linked?
- How can investigators systematically generate codes for participants in their research projects?
- Could a given institution centralise consent management in a single tool, without raising confidentiality issues?
- Can a given institution inform each patient about research projects in which their samples or data are or have been used?
- How can investigators access patient GC status, to find out whether they can reuse samples or data for each patient they would like to include?

To solve these issues, the Lausanne University Hospital (**CHUV**) has developed a consent management application, GPCR, which started being applied in April 2019.

GPCR helps investigators to manage participant recruitment. Once investigators have obtained the ethics committee's approval, they can identify their study in the application and list each recruited patient and the associated signed consent. For studies reusing data and/or samples, the GC status is automatically visible once a participant is added to a project in the application.

GPCR optimises the management of the GC. This application can help increase the number of informed patients significantly, while optimising data capture, quality, and security. Overnight, the application automatically generates mailing documents (such as cover letters and consent forms) for 1) all non-informed patients who have an appointment at the hospital within two weeks; and 2) all patients who have had an appointment within the past two weeks, and who did not get the chance to receive the documents ahead of time (in case of emergency, for instance). The GC forms that patients fill out completely and return, are then automatically registered by optical scanning. In case a patient decides later to revoke its GC, GPCR sends an e-mail notifying all investigators who have included that particular patient in their study.

GPCR also enables institutional coding system for research, which is centralised. Each patient added to GPCR receives a unique patient ID code. When a patient is then included in a research study, the application generates a new, specific patient-project ID code. Those codes are the keys for access to study data.

To conclude, GPCR as a consent management tool aims to address multiple objectives at the hospital level. It serves to fulfil some of the specific and emerging needs and concerns – of the institutional sponsors, investigators, participants, GC teams, and data scientists – regarding regulatory, security, confidentiality, data availability, and use for research-related activities.

Conclusion

The management of research consent is a major challenge in the era of personalised medicine. The three projects presented here build on the possibilities arising from digitalisation; they propose new technical solutions to current GC information, notably in an understandable way. By taking into consideration the Swiss legal requirements, the specific needs of the university hospitals involved, as well as the values and preferences of patients and citizens, these projects may significantly advance the development of digital solutions. They offer the promise of feasible methods that can be used to tailor GC, being a fundamental prerequisite for research by facilitating data exchange, sharing and interoperability. The remaining regulatory obstacles (eg. the use of electronic signature) might be solved in the future with the revision of the HRO.

A PATIENT PERSPECTIVE: TALKING ABOUT THE SWISS GENERAL CONSENT

To get an understanding of the patient perspective on the General Consent (**GC**), RA Watch Editor Séverine Méance met with Philipp do Canto from the Swiss Multiple Sclerosis Association (**MSA**).

Can you introduce yourself and the organisation(s) you represent?

I am a member of both the board and the scientific advisory board of the MSA. MSA supports people living with MS, supports scientific research, and provides its 15,000 members with independent information about their condition. I am also partner at the legal firm Public Sector Law, based in Zurich and Brussels. My focus lies on the healthcare sector, including projects in data-driven medicine.

What do you think about the need for a GC?

GC is very important for both spheres, that of the patient and of clinical research. Although not every patient is aware of the full implications of consent, GC is a fundamental element for patients as part of the regulatory and ethical approval process designed to ensure transparency and safety in all research projects. A long-lasting debate in the search for a nationally recognised standard highlights the difficulties associated with GC, but also the significance of such a declaration.

What consequences do you expect with its use?

On the positive side, I hope it will foster research and further promote Switzerland as a centre of scientific excellence. On the downside, I anticipate that the GC will continue to be perceived as a free pass for any type of use, and that patients will not be able to keep track of the use of their data.

What do you think about a national and harmonised version?

In today's scientific landscape, research is rarely carried out as single-centre studies. When a study is multicentric, the way it more often is, the use of multiple versions of GC forms may lead to an unnecessary administrative burden. Keeping in mind that medical professionals and researchers have to comply with regulation on human research on a Swiss national level (i.e. the Federal Act on Human Research or on Genetic Testing in Humans), I do not see any rationale for multiple, centre or cluster-focused versions of GC. We have one set of legal standards applied to consent – e.g. of minors, or people deemed incapable of giving consent – and clinics and patients need to therefore develop a common understanding about GC nationwide. So it is a positive sign that the major centres are working to use a common standard (i.e. the version published in February 2019).

What positive aspects do you foresee, and what could be improved?

The brevity of the current form containing two pages of information is certainly a plus. I do not think that patients in Switzerland would feel comfortable with a declaration extending over 10 pages or more, as you often find in some clinics or other European countries, such as in the UK. The disadvantage of a shorter form is, of course, its lack of precise, necessary information.

A patient may consent to one set of data being used, but not be aware that their consent could be applied to other sets of data collected during subsequent consultations, at the same hospital. This GC to use data collected at further hospital visits would then raise questions. It is possible to agree on data use if the patient is aware of its content, for instance if they were treated for a sports injury. But later on, the same patient could be treated for a sensitive illness and potentially be reluctant to grant consent. But, in reality, the already consenting patient will not be asked again for their consent. In order to address such uncertainties, the concept of dynamic consent is promising: patients should be enabled to manage their consent independently, at later stages.

Furthermore, very little explanation is given in the current GC form on the background of a standard research project. Patients may also want to know more precisely where, when, and how they can withdraw their consent. Transparency on data use (meaning its traceability and feedback on it) is merely theoretical if clinics do not provide patients with a digital interface. The technology of today allows for much more feedback to patients. In the future, it will be absolutely crucial to every person to know where and in which data set their data (e.g. their DNA profiles) is stored.

What are your perspectives about the next steps for its implementation? What are your hopes?

As a lawyer, I hope our Swiss regulator will provide clarification regarding the handling of GC, in the planned revision of research law. Although there is no need for the Federal Council to change the detailed rules on consent in the law itself, it has announced that it will address the lack of transparency and the low level of cooperation among the stakeholders in the revision of the federal ordinances on human research. This may have some implications regarding GC as it plays out in the daily operations of a clinic, such as better and technology-supported means to communicate among the parties involved.

As for the importance of data protection in the EU, we also need to closely monitor further developments abroad. Brussels will remain a strong driver for compliance and regulatory issues regarding data management in human research. Technology enables us to build bridges, crossing over into new territory, but they need to be safe enough for patients to use them.

HEADLINES AND HAPPENINGS

IN SWITZERLAND

Swiss Clinical Trial Organisation (SCTO)

● **IN 2019** the SCTO turned ten and celebrated its anniversary with the project "**People. Data. Biosamples.**" – offering an online platform for the exchange at eye level among patients, researchers, study staff, ethics committees, authorities, and the general public. Answers from experts to diverse questions will be showcased, in snappy online video portraits at 10years.scto.ch/en.

source SCTO

swissethics

● **SEPTEMBER 2019** Changes to the project registry of swissethics. Since 2016, swissethics has regularly published clinical trials and research projects that have been approved by the competent ethics committees in Switzerland. The focus was on "ongoing" clinical trials and research projects. From September on, all clinical trials/projects are to be published. Thus, the registry has been renamed RAPS: Registry of All Projects in Switzerland.

● **OCTOBER TO NOVEMBER 2019** Document Updates:
- » Recommendations and checklists for the development and operation of health-related registries
- » Template for a patient information/informed consent according to Human Research Act (**HRA**)/Human Research Ordinance (**HRO**) art. 8
- » Template for drafting information for participants in studies involving humans
- » Template of swissethics for HRO projects with persons, according to HRA/HRO ch. 2
- » Biobank regulation template

● **DECEMBER 2019** The swissethics website has a new design, with a particular attention to structure in order to find templates, guidelines, and position papers easier and faster. To share comments or questions, contact: info@swissethics.ch

● **FEBRUARY 2020** Publication of a position paper to clarify the status of either a research project to be approved by the ethics committee or a pure quality control, which according to the HRA is not subject to approval [EN]; Publication of Guiding Principles for registries in human research [DE FR]; Publication of a Template for a patient information/informed consent according to HRA/HRO art. 28 (for the further use of biological material and genetic personal data in uncoded form for a research project) [DE FR IT].

● **MARCH 2020** Publication of the annual report 2019 [DE FR]; Publication of Information on the Covid-19 [EN].

source swissethics

Kofam

● The 2018 summary report and statistical report: The Coordination Office for Human Research has the legal mandate to provide the public with information about the work of the ethics committees. Parallel to this, it has published a statistical report on the research projects that have been approved. It shows a decrease of the number of clinical trials approved in 2018 compared to 2017 (459 vs 514).
- » Summary of the individual 2018 activity reports of the ethics committees
- » 2018 statistical report on human research in Switzerland

Swissmedic

National collaboration

- The development of innovative technologies in the field of therapeutic products is advancing rapidly, posing new challenges to Swissmedic and its stakeholders. In an effort to recognise and address these challenges at an early stage, Swissmedic is establishing a Round Table Innovation as a forum for multi-stakeholder dialogue. The first meeting was held on 7 October 2019 on the topic "Decentralised Clinical Trials".

Clinical trials of medicinal products

- Clinical trial applications: Need to use white ring binders when making submissions between December 2019 and November 2020.

- Publications of updated documents:
  - **OCTOBER 2019** FO Administrative changes (including sponsorship and Swiss representative [EN]
  - **NOVEMBER 2019** FO Accompanying form for SUSARs [EN]
  - **JANUARY 2020** Working instructions for submitting changes and for reporting during the course of a clinical trial [EN]; Guideline Clinical Trial Application Dossier for medicinal products [EN]
  - **FEBRUARY 2020** FAQ on clinical trials with medicinal products [EN]; Instruction for the notification of safety measures and SUSARs in clinical trials [EN].

Medical devices

- News on the EU regulations:
  - **NOVEMBER 2019** Information regarding Eudamed. The EU commission informed about the status of the implementation of Eudamed. Currently, the launch is foreseen for May 2022.
  - **DECEMBER 2019** Second corrigendum to the Medical Devices Regulation (EU) 2017/745 (**MDR**)

- **NOVEMBER 2019** Publication of the List of Swiss medical device conformity assessment bodies [DE FR]

- **JANUARY 2020** Publication of the list of events with the participation of speakers from Swissmedic.

source Swissmedic

Federal Office of Public Health (FOPH)

- **DECEMBER 2019** Evaluation of the HRA. After the publication in the first half of 2019 of several documents concerning first findings of the evaluation of the HRA law, key documents regarding its evaluation and recommendations for its evolution followed:
  - HRA: Results of the evaluation and further action [DE FR]
  - Evaluation of the HRA: Opinion of the FOPH [DE FR]
  - Evaluation of the HRA: Final report [DE]
  - Evaluation of the HRA: Summary [EN]

The Federal Council decided to undertake a partial revision of the HRA's ordinance legislation. A bill for consultation is to be made available to the Federal Council in 2020. At the same time, measures to improve enforcement are to be defined and implemented, in coordination with the cantons and the enforcement authorities.

The following items will be at the centre of the planned revision of the ordinance:
- with regard to organising implementation, the tasks and powers of the enforcement authorities;
- in the context of research with health-related personal data and biological material, information for and consent from affected persons;
- with regard to international developments, EU legislation; and finally
- transparency in the context of the publication of research results. source FOPH

The RA Watch will closely follow the evolution of the laws and concrete consequences for human research in Switzerland.

- **JANUARY 2020** Publication of a new version of the HRA [DE FR].

- Monitoring of EU developments: As there will be implications for Switzerland, FOPH has been actively monitoring developments regarding the EU regulations on medical devices and clinical trials. Regular updates are published on its website.
  - MDR: Update November 2019; Update February 2020 [EN].
  - Clinical Trials Regulation (**EU**) No 536/2014 (**CTR**): Update December 2019; Addendum Update December 2019 [EN].

- Engaging patients is an important challenge that the FOPH is keen to support. One of the things that set the ball rolling was the Federal Council's Health2020 strategy, which explicitly places people at its centre, stating that "The health system needs to continue to develop around them and their needs". In the November 2019 edition of spectra, the FOPH team shared different levels of possible engagement, which include research and an update on ongoing projects.

Swiss Hospitals Association (H+)

● **SEPTEMBER 2019** Members of H+ support the complete revision of the ordinance on medical devices and the ordinance on clinical trials of medical devices (**ClinO-MD**), with some general reservations and provided that certain modifications are made DE FR.

unimedsuisse

● **SEPTEMBER 2019** Publication of the position paper on the proposed ordinances on medical devices. unimeduisse finds that the ClinO-MD, with its numerous references to other legal texts, lacks clarity and makes its application difficult. Without additional indications, it will be almost impossible to submit and carry out a clinical trial DE FR.

Swiss Academy of Medical Sciences (SAMS)

● **NOVEMBER 2019** The recommendations for health-related registries have been updated. Registries that provide reliable data are becoming increasingly important in the healthcare system and their number is growing. In order to guarantee their quality, the SAMS has joined forces with the ANQ, the FMH, H+, and unimedsuisse to publish recommendations on the development and operation of health-related registers: see recommendations and checklist.

● **DECEMBER 2019** Publication of SAMS's bulletin on "The power of patients". Susanne Hochuli, President of the Swiss Patient Organisation (**SPO**), explains how the SPO aims to strengthen patients and build the "fourth power" in the Swiss healthcare system. source SAMS

Swiss Biobanking Platform (SBP)

● **NOVEMBER 2019** Publication of the Biobank Information Management System guidelines, supporting the long-term operational management of biobanks.

● **NOVEMBER 2019** swissethics has endorsed the SBP Biobank Regulation. This document will replace the swissethics former template.

source SBP news

eHealth Suisse

● **DECEMBER 2019** The Electronic Patient Record (**EPR**), update on the implementation in Switzerland: As the certification procedure and formal recognition of certification bodies take longer than expected, there will be slight delays. An EPR launch across Switzerland by mid-April 2020 is unlikely. The Confederation and the cantons are nevertheless examining measures so that certain reference communities can start operating on time (if they are certified), but that the certification bodies have not yet received the accreditation. However, the entire population should be able to open an EPR by the summer of 2020 at the latest DE FR.

HEADLINES AND HAPPENINGS ABROAD

IN EUROPE

European Medicines Agency (EMA)

● **OCTOBER 2019** Update of the Informed Consent for Pediatric Clinical Trials in Europe 2015, a document collating the legal requirements in the EU member states.

● **JANUARY 2020** The EMA has agreed to the mandatory use of a consistent international format for reporting individual cases of suspected side effects in patients. The use of the new ISO individual case safety report format – which is based on the ICH E2B (R3) Guidelines – will become mandatory on 30 June 2022 for all reporting to EudraVigilance. source The Advisor, issue 455

● **JANUARY 2020** Publication of the Evolving Data-Driven Regulation report. The EMA and Heads of Medicines Agencies Joint Big Data Task Force has proposed ten priority actions for the European medicines regulatory network to ensure that it makes the best use of big data to support innovation and public health.

● **MARCH 2020** The EMA, the European Commission, and national Head of Medicines Agencies have published new recommendations for sponsors on how to manage the conduct of clinical trials in the context of the COVID-19 pandemic.

source EMA

European Commission (EC)

● **SEPTEMBER 2019** Publication of a draft document on recommendations for Preparedness of medicines' clinical trials in paediatrics.

● **OCTOBER 2019** Publication of Guidelines on Good Clinical Practice (GCP) specific to Advanced Therapy Medicinal Products. Those guidelines should be read in conjunction with the ICH E6 GCP.

● **NOVEMBER 2019** The EC has issued Eudralex 10: Application Form: Recruitment and Informed Consent Procedure Template Draft. This template has been developed and endorsed by the EU Clinical Trials Expert Group to comply with the CTR. However, this template is also relevant under Directive 2001/20/EC and may be used in advance of the regulation applying.

● **NOVEMBER 2019** CTR Draft Questions & Answers has been updated to Version 2.3.

European Parliament

● **SEPTEMBER 2019** Publication of a document commissioned by the European Parliament on How the General Data Protection Regulation (GDPR) changes the rules for scientific research.

Medicines and Healthcare products Regulatory Agency (MHRA), UK

● **JULY 2019** In a blog post, the MHRA Inspectorate highlighted some important on-site inspection findings relating to the use of electronic health records (EHRs) in clinical trials and provided guidance on how to ensure GCP compliance in this area. source MHRA

● **SEPTEMBER 2019** The UK government has committed GBP 37.5 million to make the UK a home to data-driven research, scientific advances, and innovation in healthcare to improve patient outcomes. The digital hubs will enhance the UK's ability to harness its health data to support the clinical development of new medicines. Two specific hubs will focus on clinical trials and real-world data. The hubs will link up different types of health data and make them more easily accessible and user-friendly for research, while maintaining strict controls around data privacy and consent. Patients and the public will be involved in decisions about how their data is used and accessed (source: The Advisor, issue 450).

HEADLINES AND HAPPENINGS ABROAD

INTERNATIONAL

- **OCTOBER 2019** The World Health Organization (WHO) has issued a new draft guideline that provides information, guidance, and recommendations to facilitate compliance with data integrity, GxP in documentation, and record-keeping requirements. A second public consultation is scheduled for May 2020.

- **OCTOBER 2019** Publications of three new documents on the clinical evaluations, clinical investigations and clinical evidence of medical devices by the International Medical Device Forum. This forum discusses directions for regulatory harmonisation and includes regulators from the USA, EU, and China, among other countries.

- **NOVEMBER 2019** Publication of the ICH E9 (R1) Addendum to the Guideline on Statistical Principles for Clinical Trials.

IN USA

US Food and Drug Administration (FDA)

- **OCTOBER 2019** Publication of a draft guidance on Patient-Focused Drug Development: Methods to Identify What Is Important to Patients. It describes methods to identify what matters most to patients regarding burden of disease and burden of treatment to guide medical product development, including endpoint development. This guidance is the second of a series of four methodological patient-focused drug development guidance documents developed to address – in a stepwise manner – how stakeholders can collect and submit patient experience data and other relevant information from patients and caregivers, to use in medical product development and regulatory decision-making. The first guidance document finalised, Patient-Focused Drug Development: Collecting Comprehensive and Representative Input should be published early of 2020.

- **NOVEMBER 2019** Publication of final guidance on Adaptive Designs for Clinical Trials of Drugs and Biologics. The guidance describes important principles for designing, conducting, and reporting the results from an adaptive clinical trial.

- **DECEMBER 2019** Publication of a new draft guidance document entitled Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products. The new guidance states that the substantial evidence requirement for effectiveness – which had generally been interpreted as calling for two adequate and well controlled trials – could also be met by a single trial plus confirmatory evidence.

- **JANUARY 2020** Publication of seven guidance documents to support innovation in development of Gene Therapy Products. By 2025, the FDA expects it will be reviewing and approving between 10 and 20 cell and gene therapies each year.

EVENTS AND PUBLICATIONS

Events

11–13 MAY 2020

RAPS Regulatory Conference Europe
BRUSSELS

27 MAY 2020

Networking event: clinical ethics in Switzerland
Event organised by the SAMS.
BERN

20-21 SEPTEMBER 2021

D-A-CH symposium
Three-nation congress on clinical trials in Germany, Austria and Switzerland.
SALZBURG, AUSTRIA

DATE TO BE CONFIRMED

Symposium: Medical devices: lost in translation?
Event organised by the SCTO in collaboration with the Bern University Hospital, the University of Bern and the Swiss Institute for Translational and Entrepreneurial Medicine.
BERN

Note: Events might be rescheduled or cancelled due to current happenings.

Books and publications

- Santel F. et al., "Assessing readability and comprehension of informed consent materials for medical device research: **A survey of informed consents from FDA's Center for Devices and Radiological Health**". Contemporary Clinical Trials, Volume 85, 2019, 105831. The investigators believe that information about informed consent forms' readability, comprehension, and structure will help support current and future efforts to improve the informed consent process.
- Pundir N et al., "**Delving into eConsent: Industry Survey Reinforces Patient Centricity**". Clinical Researcher, Volume 34, Issue 1, January 2020 (The Association of Clinical Research Professionals website).
- Perry B. et al., "Patient preferences for using mobile technologies in clinical trials". Contemporary Clinical Trials Communications, Volume 15, September 2019, 100399. The majority of survey respondents reported that they would prefer participating in a clinical trial that used mobile technology than a traditional trial that relied on standard in-clinic assessments.
- Devito N. et al., "Compliance with legal requirement to report clinical trial results on ClinicalTrials.gov: a cohort study". The Lancet, Volume 395, Issue 10221, 1–7 February 2020, Pages 361-369. The study shows that the majority of sponsors fail to report the results of studies before the publication deadline with the non-industry most likely to fail.
- Leslie Sam, principal consultant, Wool Consulting Group. "The Revised ICH E8: A Guide to New Clinical Trial Requirements". With ICH E8(R1) set to be adopted in June 2020, your planning, design and conduct of clinical trials will look different than they do today. This guide may help you implement the new guidelines.

ACRONYMS

C3-STuDY: Citizen Centered Consent: Shared, Transparent and Dynamic
CHUV: Centre Hospitalier Universitaire Vaudois (Lausanne University Hospital)
ClinO: Ordinance on Clinical Trials
CTR: Clinical Trials Regulation (EU) 536/2014
CTU: Clinical Trial Unit
EC: European Commission
EMA: European Medicines Agency
EPR: Electronic Patient Record
EU: European Union
FDA: Food and Drug Administration
FOPH: Federal Office of Public Health
GC: General Consent
GCP: Good Clinical Practice
GDPR: General Data Protection Regulation (EU) 2016/679
GPCR: Gestion Proactive des Consentements de Recherche
H+: Swiss Hospitals Association
HRA: Human Research Act
HRO: Human Research Ordinance
HUG: Hôpitaux Universitaires Genève
IC: Informed Consent
ICH: International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
MDR: Medical Devices Regulation (EU) 2017/745
MHRA: Medicines and Healthcare products Regulatory Agency
MSA: Multiple Sclerosis Association
ClinO-MD: Ordinance on Clinical Trials of Medical Devices
SAMS: Swiss Academy of Medical Science
SBP: Swiss Biobanking Platform
SCTO: Swiss Clinical Trial Organisation
SERI: State Secretariat for Education, Research and Innovation
SPHN: Swiss Personalized Health Network
SBP: Swiss Biokanking Platform
SPO: Swiss Patient Organisation
SwissPedNet: Swiss Research Network of Clinical Pediatric Hubs
TPA: Therapeutic Products Act
WHO: World Health Organization

REGULATORY AFFAIRS WATCH

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Sources of information

- We gather news on regulatory topics linked to human research.
- We regularly read newsletters and visit the websites of relevant sources, including: the regulatory authorities in Switzerland, Europe, and USA; ICH and WHO; the major Swiss academic organisations and health associations; and professional associations.
- Additionally, we review major clinical research journals.

More on the Regulatory Affairs Platform

https://scto.ch/en/network/scto-platforms/regulatory-affairs.html

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The Swiss Clinical Orgnisation (**SCTO**), together with partner organisations, hosts thematic platforms to promote excellence in clinical research in Switzerland. **www.scto.ch**