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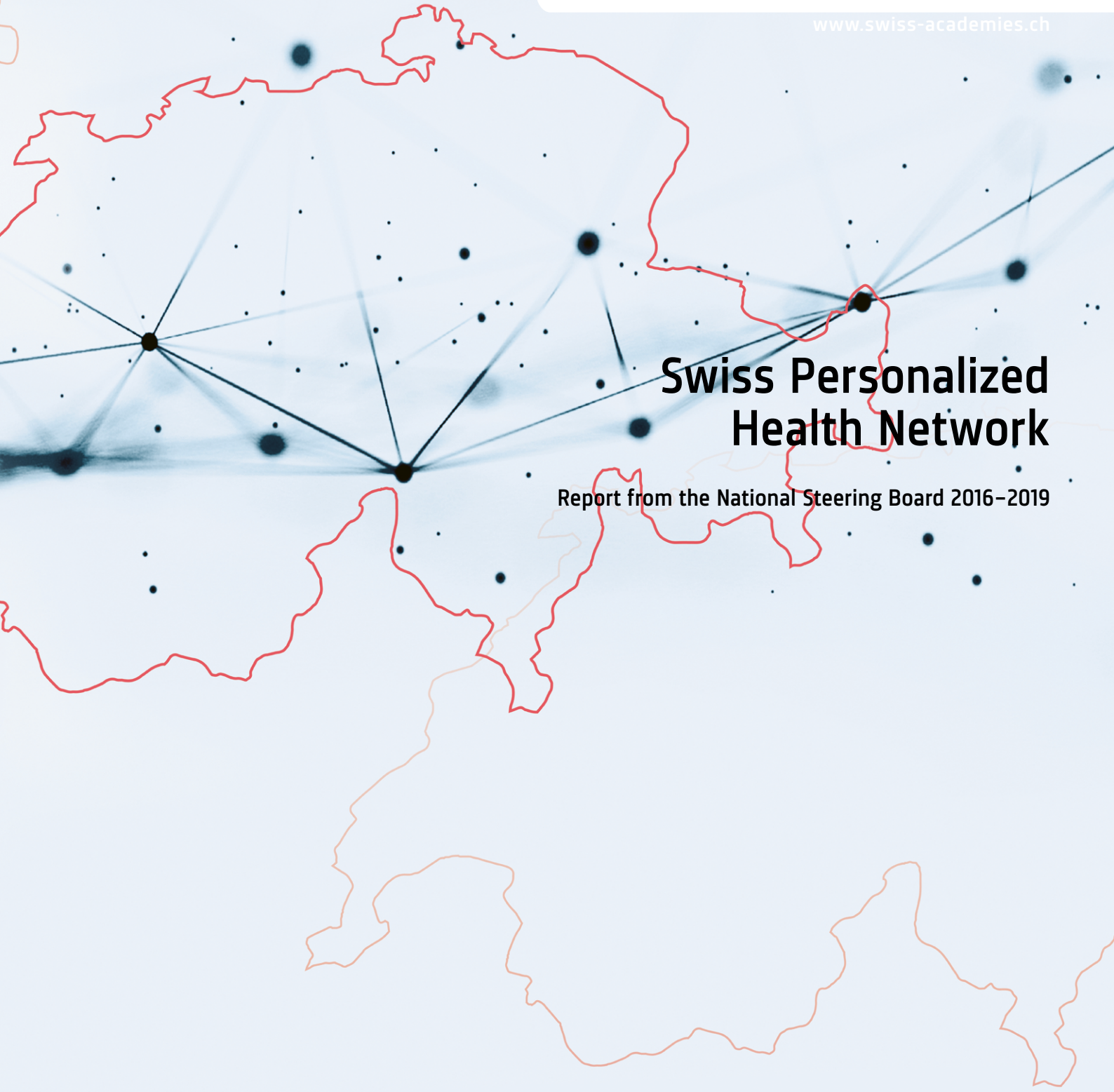

Swiss Personalized Health Network

Report from the National Steering Board 2016–2019

A project of

SAMW ASSM

Schweizerische Akademie der Medizinischen Wissenschaften
Académie Suisse des Sciences Médicales
Accademia Svizzera delle Scienze Mediche
Swiss Academy of Medical Sciences

SIB Swiss Institute of Bioinformatics

Information on the preparation of the report

During the year 2019, an initial mapping and gap analysis was performed based on the annual reports submitted by the SPHN-funded projects and Collaboration Agreements signed with the University Hospitals. This mid-term analysis allowed progress to be measured and the creation of a national map, indicating which types of infrastructures (platforms, algorithms, document templates etc.) are available or under development for personalized health research in Switzerland. At the same time, a two-day Review Meeting was organized in September 2019, providing the International Advisory Board (IAB) of SPHN with the opportunity to hear about the achievements of SPHN-funded projects and works of the University Hospitals, but also about the challenges and hurdles encountered. On this basis, almost three years after its operational launch, the IAB provided a first in-depth review of the initiative as a whole, identifying the successes but also the gaps with a particular need for action.

During its meeting in September 2019, Urs Frey, chair of the National Steering Board (NSB), first presented the idea to elaborate a detailed progress report based on this overall mid-term review and feedback of the IAB. Following endorsement of the proposition by the NSB, a small Writing Group, composed of Prof. Urs Frey, Chair NSB; Dr. Adrien Lawrence, Managing Director SPHN; Dr. Katrin Crameri, Head of Personalized Health Informatics Group; Prof. Torsten Schwede, Chair National Advisory Board; Dr. Sabine Oesterle, Personalized Health Informatics Group and Dr. Liselotte Selter, SPHN Management Office, developed a first version of the «Swiss Personalized Health Report from the National Steering Board 2016–2019», which was submitted to the NSB for its meeting in February 2020 with an invitation to provide feedback. Following consolidation of the comments, a prefinalized version was submitted to and approved for publication by the NSB during its meeting in May 2020. Given that in the meantime the National Advisory Board (NAB) of SPHN (composed of experts in the infrastructural aspects of the initiative) was formed, members of the NAB were also given the opportunity to comment on the report.

The finalized version was shared with the NSB at its meeting on 17 September 2020 and processed for publication as a Swiss Academies Report.

The authors expect to develop a targeted publication (e.g., in a medical journal [FMH, SMW…]) based on this report to further increase the visibility of the initiative.

Swiss Personalized Health Network

Report from the National Steering Board 2016–2019

IMPRINT

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Foreword

With its high-quality healthcare network and excellence in research and innovation, Switzerland has the potential to become one of the European leaders in healthcare and biomedical science. Translating this potential into reality can bring the Swiss healthcare system to the next level, allowing data-driven precision medicine and fostering personalized health. This ambitious vision requires structural evolution in the data landscape. With the progress made in other leading nations in the world, these changes can no longer be considered as optional without hindering Switzerland's competitiveness.

Given the tremendous amount of health data already available, healthcare and medical decisions should no longer be based solely on cohort averages, but take into account individual patient characteristics, including the variability in genes, molecular biomarkers, environment and lifestyle. To leverage the immense potential of data for better prevention, improved medical practice and ground-breaking innovative treatments, transdisciplinary scientific research, as well as specific infrastructural efforts are necessary: health data needs to be interoperable and broadly accessible for research. Additionally, health-data research requires cutting-edge IT infrastructures fulfilling stringent data protection and information security requirements.

To this end, the Swiss Personalized Health Network (SPHN) initiative was launched in 2017, with the mission to collaboratively advance personalized health research and innovation by building upon – and supporting – existing data sources and infrastructures across the country. During the past three years, nationwide coordinated infrastructures have been set up in order to efficiently manage, exchange and process consented health data in accordance with ethical and legal requirements. In collaboration with the SIB Swiss Institute of Bioinformatics, the ETH Domain, the Universities and the University Hospitals, SPHN allows the linkage of coded patient data with data deriving from the latest analytical platforms, e.g., in the field of genomics, metabolomics and proteomics. SPHN stringently coordinates its efforts with partner networks such as the Personalized Health and Related Technologies initiative of the ETH Domain (PHRT), the Swiss Biobanking Platform (SBP), the Swiss Clinical Trial Organisation (SCTO) and patient-citizen organizations.

This report gives an overview of the current status of the network development, highlights the conceptual changes introduced by SPHN and presents the results of a gap analysis and international review, carried out by SPHN in Summer 2019. The major challenges to come will be the real-world implementation of SPHN infrastructures, adoption of harmonized standards, processes and data-sharing principles. There is a need for collaborative efforts, open discussions and involvement of multiple stakeholders, including patient and citizen representatives. Although representatives of patient organizations have been involved in the SPHN ELSI advisory group and in the National Steering Board since the beginning of the initiative, their voice needs to be strengthened. Indeed, public trust, understanding the risks and benefits, and consequently willingness to share data to progress science and healthcare in Switzerland are important prerequisites for the success of the initiative.

Prof. Urs Frey
Chairperson, SPHN National Steering Board

Keywords
#HealthDataManagement, #PrecisionMedicine, #PersonalizedHealth, #HealthResearchInfrastructure, #SPHN, #DataDrivenMedicine, #GeneralConsent, #BroadConsent, #PatientInvolvement

Executive Summary – English

Personalized medicine is a research trend in patient-oriented research which has been evolving for nearly two decades and is likely to continue transforming our future healthcare. With its high-quality healthcare network and excellence in research and innovation, Switzerland has the potential to become one of the European leaders in health and biomedical science. In order to make this vision a reality and remain internationally competitive, the build-up of a sustainable, personalized medicine ecosystem in Switzerland is a prerequisite and requires a joint venture between citizens, researchers, healthcare providers, authorities and cooperation partners.

The Swiss Personalized Health Network (SPHN) initiative was launched in 2017 by the Swiss Federal Government (State Secretariat for Education, Research and Innovation [SERI] and the Federal Office of Public Health [FOPH]) as a first step to facilitating research in such a future ecosystem. The Swiss Academy of Medical Sciences (SAMS), in collaboration with the SIB Swiss Institute of Bioinformatics, is responsible for the implementation of the mandate, which has been allocated a total of CHF 68 Mio for the period 2017–2020. A second funding period of the initiative is ensured for 2021–2024, following which the developed research infrastructures should be self-sustainable.

It is the mission of SPHN to collaboratively advance personalized health research and innovation by building upon – and supporting – existing data sources and infrastructures across the country. For the first funding period, 2017–2020, the focus lied on the development of a nationally coordinated research data infrastructure, including interoperability of local and regional information systems.

In order to optimize and leverage the use of primarily clinical but also other health-related data for personalized health research, both transdisciplinary scientific research as well as specific infrastructural efforts are necessary: we need to create infrastructures allowing rapid and broad access to consented and ethically approved, fit-for-purpose, interoperable and standardized healthcare data, which can be linked to cutting-edge IT infrastructures, research platforms and biobanks fulfilling stringent data protection and information security requirements.

While the first infrastructures are – at least in the first SPHN phase – primarily developed in the Swiss University Hospitals, the latter infrastructures are heavily developed by our partner organizations ETH with its Personalized Health and Related Technologies (PHRT) initiative, the SNSF-funded Swiss Biobanking Platform (SBP), the universities, the hospitals and many other health-related research partners. By facilitating the dialogue between these relevant stakeholders, we aim to establish a reputation as a trusted research partner network.

In order to streamline and harmonize at least parts of this development and to make health data from University Hospitals sharable and effectively usable for research, a mixed top-down and bottom-up approach was chosen. On the one hand, Collaboration Agreements (Infrastructure implementation projects) between SPHN and each Swiss University Hospital were signed, with the aim of developing systems that allow interoperable data exchange at all five institutions. On the other hand, SPHN launched two calls for proposals in 2017 and 2018 to fund two types of projects: “Infrastructure Development Projects”, aiming to develop and test new technologies, methods and infrastructures and “Driver Projects”, guiding the development of SPHN by test-driving the infrastructures and interoperability for multi-site research in a specific area or pathology.

The SPHN Data Coordination Center (DCC) operated by the Personalized Health Informatics Group of the SIB Swiss Institute of Bioinformatics is key to reaching the interoperability goals of the initiative. Its mandate is to promote the development and implementation of nationwide standards for data semantics and exchange mechanisms and therefore it closely collaborates with its various technical expert working groups. In addition, the DCC coordinates the implementation of the key milestones of the collaboration agreements as well as the BioMedIT network. The latter was funded by the Swiss Federal Government for the period 2017–2020 as part of the Swiss Roadmap for Research Infrastructures within the framework of SPHN and PHRT and has been specifically designed for collaborative research projects on sensitive data that are brought together from different data sources and analysed by multidisciplinary research teams from different institutions.

This report gives an overview of the current status of the network development, highlights the conceptual changes introduced by SPHN and presents the results of a gap analysis and international review, carried out by SPHN during the year 2019. It further provides an outlook into the funding period 2021–2024 and critically reflects the progress of the initiative as well as the problems identified.

During the past three years, not only have SPHN's governance, working principles and frameworks been defined, but also nationwide coordinated infrastructures have been built up in order to efficiently manage, exchange and process consented health data in accordance with ethical and legal requirements. The funding period 2017–2020 was further instrumental for stakeholder alignment, process innovation, definition and harmonization of standards and interoperability. The biggest achievement of this period however, is probably the increasing awareness of the systemic gaps and problems of big-data health science in Switzerland, which were revealed by the SPHN Driver Projects.

These problems are mainly related to the complexity of data influencing health as well as the heterogeneity of the Swiss health system with its local legal, ethical and regulatory frameworks. Interoperability, and thus big-data health science, is critically dependent on nationwide harmonization of these regulatory frameworks. The need for alignment and coordination of the efforts has become imminent for all stakeholders and their willingness to agree and implement common strategies, standards and guidelines will be a prerequisite for the initiative's success and possibly require a discussion at the political level.

In view of the next funding period 2021–2024, using the acquired knowledge of this Gap Analysis, the major challenges to come will be the real-world implementation and consolidation of SPHN infrastructures, as well as the adoption of harmonized standards, processes and data-sharing principles. In order to ensure sustainability and scalability of the nationally coordinated health-data research infrastructures built up by SPHN and its partners, stringent and coordinated implementation strategies and public dialogue will be key efforts. There is, however, much to win: a data-driven landscape is a transformation instrument that has the potential to evolve a traditional healthcare system towards a learning, efficient, qualitative and personalized care system. This transformation of the core functioning of the care system will be of benefit for all stakeholders – primarily citizens, but also governing bodies, public health organizations and the research community.

Executive Summary – Deutsch

Personalisierte Medizin hat sich in den letzten zwei Jahrzenten als eine Entwicklung in der patientenorientierten Forschung etabliert, die mit grosser Wahrscheinlichkeit auch in Zukunft unsere Gesundheitsversorgung verändern wird. Die Schweiz hat dank ihrer exzellenten Forschung, Innovationskraft und ihrem qualitativ hochstehenden Gesundheitssystem gute Chancen, zu den führenden europäischen Ländern im Bereich biomedizinische Forschung und Gesundheitsforschung zu zählen. Diese Vision zu verwirklichen und international wettbewerbsfähig zu bleiben, setzt den Aufbau eines nachhaltigen Ökosystems in personalisierter Medizin voraus – und zwar als Gemeinschaftsprojekt zwischen Bürger/-innen, Forschenden, Gesundheitsdienstleistern, Behörden und Kooperationspartnern.

Die Swiss Personalized Health Network (SPHN) Initiative wurde 2017 im Auftrag des Bundes lanciert (Staatssekretariat für Bildung, Forschung und Innovation und Bundesamt für Gesundheit), um in einem ersten Schritt die Forschung in einem solchen Ökosystem zu unterstützen. Die Schweizerische Akademie der Medizinischen Wissenschaften (SAMW) ist, in Zusammenarbeit mit dem Schweizerischen Institut für Bioinformatik SIB, für die Umsetzung verantwortlich. Insgesamt 68 Mio. Franken wurden für den Zeitraum 2017–2020 bereitgestellt, eine zweite Förderperiode ist für die Jahre 2021–2024 gesichert. Danach sollen die entwickelten Forschungsinfrastrukturen selbsttragend sein.

Das gemeinsame Vorantreiben von Forschung und Innovation im Bereich personalisierte Gesundheit, basierend auf bereits bestehenden, nationalen Datenquellen und Infrastrukturen und deren Weiterentwicklung, stellt den Kern des SPHN-Auftrags dar. Fokus der ersten Förderperiode 2017–2020 war die Entwicklung einer national koordinierten Forschungsdateninfrastruktur, einschliesslich der Interoperabilität lokaler und regionaler Informationssysteme.

Um die Nutzung von klinischen, aber auch anderen gesundheitsrelevanten Daten für die personalisierte Gesundheitsforschung zu optimieren, sind sowohl transdisziplinäre wissenschaftliche Forschung als auch spezifische infrastrukturelle Anstrengungen notwendig. Es müssen Plattformen geschaffen werden, die einen schnellen und breiten Zugang zu standardisierten, interoperablen und zweckmässigen Gesundheitsdaten ermöglichen, für deren Nutzung zu Forschungszwecken die Einwilligung der Betroffenen sowie der verantwortlichen Ethikkommissionen vorliegen. Diese Infrastrukturen müssen ausserdem mit Hochleistungs-Rechenzentren, Forschungsplattformen und Biobanken verknüpft werden können, die den hohen Anforderungen an Datenschutz und Informationssicherheit genügen.

Während der ersten Finanzierungsperiode des SPHN haben die Schweizer Universitätsspitäler bei der Entwicklung dieser Infrastrukturen eine zentrale Rolle gespielt. Die Partnerorganisationen des SPHN, etwa die Initiative «Personalized Health and Related Technologies (PHRT)» des ETH-Bereichs, die vom Schweizer Nationalfonds finanzierte Swiss Biobanking Platform (SBP), die Universitäten, Spitäler und viele andere gesundheitsbezogene Forschungspartner treiben dagegen die Entwicklung moderner Rechenzentren, Forschungsplattformen und Biobanken voran. Indem der Dialog zwischen diesen relevanten Akteuren gefördert und erleichtert wird, will sich SPHN einen Ruf als vertrauenswürdiges Forschungspartnernetzwerk aufbauen.

Um diese Entwicklung zu koordinieren und Gesundheitsdaten von Universitätsspitälern austauschbar und effektiv für die Forschung nutzbar zu machen, hat SPHN sowohl einen Top-Down- als auch Bottom-Up-Ansatz gewählt. Einerseits wurden Leistungsvereinbarungen (Infrastruktur-Implementierungsprojekte) zwischen SPHN und den fünf Schweizer Universitätsspitälern unterzeichnet, um Systeme zu entwickeln, die einen interoperablen Datenaustausch zwischen den Institutionen ermöglichen. Andererseits lancierte SPHN in den Jahren 2017 und 2018 Ausschreibungen zur Finanzierung von zwei Projektentypen: Die Infrastructure Development Projects haben zum Ziel, neue Technologien, Methoden und Infrastrukturen für Forschung im Bereich personalisierter Gesundheit zu entwickeln und zu testen. Die Driver Projects sind in einem konkreten Forschungsgebiet oder einer Pathologie angesiedelt. Sie sollen die Entwicklung von klinischen Datenmanagementsystemen in mehreren Universitätsspitälern vorantreiben, indem Dateninteroperabilität und Grundsätze der gemeinsamen Datennutzung im gesamten Netzwerk getestet werden.

Das von der Personalized Health Informatics Group des SIB betreute Data Coordination Center (DCC) ist für das Erreichen der Interoperabilitätsziele innerhalb SPHN zentral. Es hat den Auftrag, die Entwicklung und Umsetzung von landesweiten Standards für Datensemantik und Austauschmechanismen zu fördern. Für die ihm zugewiesenen Aufgaben arbeitet es eng mit verschiedenen technischen Expertenarbeitsgruppen zusammen. Darüber hinaus koordiniert das DCC die Umsetzung

der in den Leistungsvereinbarungen mit den Universitätsspitälern definierten Meilensteine und das BioMedIT-Netzwerk. Letzteres wurde vom Bund für den Zeitraum 2017–2020 als Teil der Schweizer Roadmap für Forschungsinfrastrukturen und integraler Teil der SPHN- und PHRT-Initiativen finanziert. Das BioMedIT-Netzwerk ist speziell für Forschungsprojekte mit sensiblen Daten konzipiert, die aus unterschiedlichen Datenquellen zusammengeführt und von multidisziplinären Forschungsteams aus verschiedenen Institutionen analysiert werden.

Dieser Bericht gibt einen Überblick über den Stand der Netzwerksentwicklung. Insbesondere beleuchtet er die durch SPHN geschaffenen konzeptionellen Veränderungen und präsentiert die Ergebnisse der 2019 durchgeführten Gap-Analyse und Begutachtung durch das internationale SPHN-Expertengremium. Der Bericht liefert ausserdem einen Ausblick auf die Förderperiode 2021–2024 und reflektiert kritisch die Fortschritte und die identifizierten Hürden und Herausforderungen.

In den drei Jahren operativer Tätigkeit wurden nicht nur die Governance, die Arbeitsprinzipien und Rahmenbedingungen von SPHN definiert, sondern auch landesweit koordinierte Infrastrukturen aufgebaut. Dies, um Gesundheitsdaten mit vorliegender Einwilligung zu Forschungszwecken im Einklang mit ethischen und rechtlichen Anforderungen effizient zu verwalten, auszutauschen und zu verarbeiten. Die Förderperiode 2017–2020 war ausserdem entscheidend für die Angleichung der diversen Interessengruppen hinsichtlich Prozessinnovation, Definition und Harmonisierung von Standards und Interoperabilität. Die wohl grösste Errungenschaft dieser ersten Phase besteht jedoch darin, dass die systemischen Lücken und Herausforderungen der Big-Data-Gesundheitsforschung in der Schweiz durch die Driver Projects zum Vorschein gebracht wurden und dies zu einer zunehmenden Sensibilisierung und einem gemeinsamen Bewusstsein der Netzwerkpartner geführt hat.

Die Herausforderungen und bestehenden Lücken hängen einerseits damit zusammen, dass Daten, die unsere Gesundheit beeinflussen, sehr komplex sind. Andererseits, dass das heterogene Schweizer Gesundheitssystem mit seinen lokalen rechtlichen, ethischen und regulatorischen Rahmenbedingungen signifikante Hürden für die Gesundheitsforschung mit grossen Datenmengen darstellt. Eine landesweite Harmonisierung der rechtlichen Rahmenbedingungen ist für die Interoperabilität und somit den Erfolg von Big-Data-Gesundheitsforschung entscheidend. Den Beteiligten ist die dringende Notwendigkeit einer besseren und effizienteren Koordination der vielfältigen, bereits bestehenden Bemühungen in diesem Gebiet bewusst. Die Bereitschaft aller Beteiligten, Vereinbarungen hinsichtlich gemeinsamer Strategien, Standards und Richtlinien sowie deren Umsetzung zu treffen, ist eine grundlegende Voraussetzung für den Erfolg der Initiative. Möglicherweise ist hierzu auch eine Diskussion auf politischer Ebene erforderlich.

Basierend auf den Erkenntnissen der Gap-Analyse und im Hinblick auf die nächste Förderperiode 2021–2024 sind die grössten Herausforderungen erstens in der realen Umsetzung und Konsolidierung der SPHN-Infrastrukturen und zweitens in der Annahme harmonisierter Standards, Prozesse und Prinzipien für den Datenaustausch zu erwarten. Um die Nachhaltigkeit und Skalierbarkeit der von SPHN und seinen Partnern aufgebauten, national koordinierten Gesundheitsdaten-Forschungsinfrastrukturen zu gewährleisten, werden stringente und abgestimmte Implementierungsstrategien und der öffentliche Dialog im Mittelpunkt stehen. Der mögliche Gewinn ist gross: Eine datengetriebene Gesundheitsforschung hat das Potenzial, ein traditionelles Gesundheitssystem in ein qualitatives, effizientes, lernendes und personalisiertes Versorgungssystem zu transformieren. Eine solche Transformation der Kernfunktionen des Versorgungssystems ist für alle Interessengruppen von Nutzen – in erster Linie für Bürgerinnen und Bürger bzw. Patientinnen und Patienten, aber auch für Verwaltungsorgane, die Organisationen des öffentlichen Gesundheitswesens und die Forschungsgemeinschaft.

Executive Summary – Français

La médecine personnalisée s'est établie au cours des deux dernières décennies comme une évolution dans la recherche orientée vers le patient qui modifiera très probablement la prise en charge médicale du futur. Grâce à son excellente recherche, sa force d'innovation et la qualité de son système de santé, la Suisse a de grandes chances de compter parmi les leaders européens dans le domaine de la recherche biomédicale et de la recherche en santé. Pour concrétiser cette vision et rester compétitif sur le plan international, il est nécessaire de développer un écosystème durable dans le domaine de la médecine personnalisée – sous la forme d'un projet commun porté par la population, la communauté scientifique, les prestataires de soins, les autorités et les institutions partenaires.

L'initiative Swiss Personalized Health Network (SPHN) a été lancée en 2017 à la demande de la Confédération (Secrétariat d'État à la formation, à la recherche et à l'innovation et Office fédéral de la santé publique), afin de soutenir dans une première étape la recherche dans un tel écosystème. L'Académie Suisse des Sciences Médicales (ASSM) est responsable de la mise en œuvre du projet en collaboration avec le SIB Institut suisse de bioinformatique. Un montant total de 68 millions a été mis à disposition pour la période de 2017 à 2020; une deuxième période de financement est assurée pour les années 2021 à 2024. Par la suite, les infrastructures de recherche ainsi développées devront être financièrement autonomes.

La promotion de la recherche et de l'innovation dans le domaine de la santé personnalisée, basée sur les sources de données et les infrastructures nationales existantes et leur développement ultérieur, est au cœur de la mission du SPHN. La première période de financement 2017–2020 a été consacrée au développement d'une infrastructure de données de recherche coordonnée au niveau national, incluant l'interopérabilité des systèmes d'information locaux et régionaux.

Afin d'optimiser l'exploitation des données cliniques, mais également d'autres données de santé pertinentes pour la recherche en santé personnalisée, il faut à la fois une recherche scientifique transdisciplinaire et des efforts infrastructurels spécifiques. Des plateformes permettant un accès rapide et élargi à des données de santé standardisées, interopérables et adéquates doivent être créées; l'utilisation de ces données à des fins de recherche requiert le consentement des personnes concernées et des commissions d'éthique responsables. Ces infrastructures doivent, par ailleurs, être reliées à des centres de données de haute performance, des plateformes de recherche et des biobanques qui répondent aux exigences élevées de la protection des données et de la sécurité de l'information.

Pendant la première période de financement du SPHN, les hôpitaux universitaires suisses ont joué un rôle central dans le développement de ces infrastructures. De leur côté, les organisations partenaires du SPHN, comme l'initiative « Personalized Health and Related Technologies (PHRT) » du domaine des EPF, la Swiss Biobanking Platform (SBP) financée par le Fonds National Suisse, les universités, les hôpitaux et de nombreux autres partenaires de recherche dans le domaine de la santé favorisent le développement de centres informatiques, de plateformes de recherche et de biobanques modernes. En encourageant et en facilitant le dialogue entre ces acteurs essentiels, le SPHN souhaite se forger une réputation de catalysateur de confiance pour la mise en réseau des partenaires de recherche.

Afin de coordonner ce développement et de rendre les données de santé des hôpitaux universitaires échangeables et utilisables pour la recherche, le SPHN a choisi une approche à la fois « top-down » et « bottom-up ». D'une part, des accords de prestations (projet d'implémentation d'infrastructures) entre le SPHN et les cinq hôpitaux universitaires suisse ont été signés, pour développer des systèmes permettant un échange de données interopérables entre les différentes institutions. D'autre part, le SPHN a lancé en 2017 et 2018 des mises au concours pour le financement de deux types de projets : les « Infrastructure Development Projects » et les « Driver projects ». Les premiers sont destinés au développement et à l'évaluation des nouvelles technologies, méthodes et infrastructures pour la recherche en médecine personnalisée. Les seconds portent sur une pathologie ou un domaine de recherche concret, dont l'objectif est de faire progresser le développement de systèmes de gestion de données cliniques dans plusieurs hôpitaux universitaires en testant l'interopérabilité et les principes de l'utilisation conjointe des données dans l'ensemble du réseau.

Le Data Coordination Center (DCC) géré par le Personalized Health Informatics Group du SIB est essentiel pour atteindre les objectifs d'interopérabilité au sein du SPHN. Sa mission est de promouvoir le développement et la mise en œuvre de standards nationaux pour la sémantique des données et les mécanismes d'échanges. Pour

ce faire, il travaille en collaboration étroite avec différents groupes d'experts techniques. Par ailleurs, le DCC coordonne la mise en œuvre des jalons définis dans les accords de prestations avec les hôpitaux universitaires et le réseau BioMedIT. Ce dernier a été financé par la Confédération pour la période 2017–2020 dans le cadre de la feuille de route suisse pour les infrastructures de recherche et fait partie intégrante des initiatives SPHN et PHRT. Le réseau BioMedIT a été conçu spécialement pour les projets de recherche contenant des données sensibles, provenant de diverses sources qui sont analysées par des équipes de recherche multidisciplinaires de différentes institutions.

Le rapport donne un aperçu de l'état actuel du développement du réseau. Il expose notamment les changements conceptuels introduits par le SPHN et présente les résultats de l'analyse des lacunes (« gap analysis ») réalisée en 2019 et l'évaluation par le comité international d'experts du SPHN. Le rapport donne, par ailleurs, un aperçu de la période de financement 2021–2024 et se livre à une réflexion critique sur les progrès réalisés et les obstacles et défis identifiés.

Ces trois ans d'activité opérationnelle ont permis non seulement de définir la gouvernance, les principes de travail et les conditions cadres du SPHN, mais également de mettre en place des infrastructures nationales coordonnées. Ceci avec l'objectif de gérer, d'échanger et de traiter efficacement les données de santé mises à disposition à des fins de recherche avec le consentement préalable du patient et en accord avec les exigences éthiques et juridiques. La période de financement 2017–2020 a, par ailleurs, été décisive pour concilier les groupes d'intérêt divergents en termes d'innovation de processus, de définition et d'harmonisation des normes et de l'interopérabilité. Cependant, la réalisation la plus importante de cette première phase a probablement été de mettre en évidence, grâce aux Driver Projects, les lacunes et les enjeux systémiques de la recherche en santé fondée sur les Big Data en Suisse et, ainsi, d'accroître la sensibilisation et de promouvoir une prise de conscience commune parmi les partenaires du réseau.

Les défis et les lacunes existantes sont attribués, d'une part, au fait que les données qui influencent notre santé sont très complexes, et, d'autre part, au système de santé suisse très hétérogène avec ses conditions cadres juridiques, éthiques et réglementaires locales qui sont des obstacles significatifs pour la recherche sur la santé avec de grandes quantités de données. Une harmonisation nationale des conditions cadres juridiques est indispensable à l'interopérabilité et donc au succès de la recherche en santé basée sur les Big Data. Les partenaires concernés sont conscients de la nécessité impérieuse d'une coordination plus efficace des efforts entrepris dans ce domaine. La volonté de tous les participants de conclure des accords concernant des stratégies communes, des normes et des directives ainsi que leur mise en œuvre, est une condition préalable fondamentale au succès de l'initiative. Un débat au niveau politique peut s'avérer nécessaire à cet égard.

Basé sur les résultats de la « gap analysis » et dans l'optique de la prochaine période de financement 2021–2024, les principaux défis résident premièrement dans la mise en œuvre effective et dans la consolidation des infrastructures du SPHN et deuxièmement dans l'adoption de standards, de processus et de principes harmonisés pour l'échange des données. Le SPHN et ses partenaires ont développé des infrastructures de recherche sur les données de santé coordonnées au niveau national; afin d'assurer leur durabilité et leur évolutivité, l'élaboration de stratégies d'implémentation rigoureuses et définies en concertation ainsi qu'un dialogue avec le public seront essentiels. Le bénéfice possible est énorme : la recherche en santé fondée sur les données a le potentiel de transformer le système de santé traditionnel en un système de santé de qualité, efficace, capable d'améliorations et personnalisé. Une telle transformation des fonctions clés du système de santé est au bénéfice de tous les groupes d'intérêt – en premier lieu des citoyennes et citoyens respectivement des patientes et des patients, mais également des organes administratifs, des organisations du système de santé public et de la communauté scientifique.

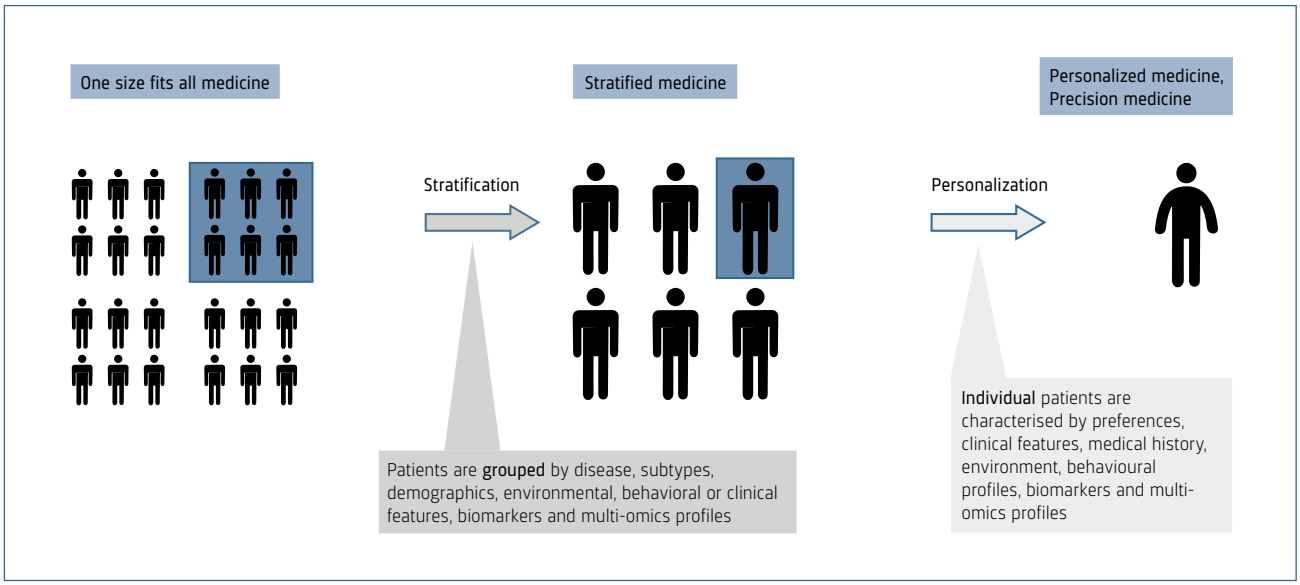
1. Introduction

Personalized health is a research trend in patient-oriented research, which has been evolving for nearly two decades, and will likely dominate the healthcare of this century, including significant changes in healthcare, biomedical-research infrastructures and health economy. It is based on the concept of precision medicine and the notion that in many diseases, a more accurate phenotyping of the patient including biomarkers such as environmental, clinical, physiological, genetic, metabolic or protein profiles can result in better and often more specific patient treatment or risk and outcome prediction. This has become obvious in the field of monogenetic diseases, where the identification of specific genes or metabolic pathways can allow specific treatments even in individual patients (Figure 1). While these situations are still rare, there is increasing evidence in a variety of chronic diseases (such as asthma, diabetes and cancer), where subgroups or subphenotypes can profit from specific treatments. This stratifying approach can not only have a significant impact on the healthcare of the individual patient, but also on the health economic aspects of the healthcare system.

However, research in this specific field requires certain conditions, which are often not available in the current healthcare system and research landscape. These are:

- Availability of standardized, analytical methods;
- Patient data, which allow accurate and standardized clinical phenotyping;
- Standardized assessment of such clinical and analytical data not only in individual institutions but in national and even international research networks;
- Processes allowing the aggregation of large data sets of patient and citizen health data;
- Interoperability of data, standardized semantics, bioinformatics for big-data-analysis, quality standards;
- Established standard operating procedures and process innovations, regulatory framework facilitating scientific research;
- Legally and ethically compliant and technically secured data sampling, acquisition, transport, storage and treatment, including mechanisms for patient consent and data protection (appropriate security measures, codes of conduct, researcher accountability);
- Public trust, understanding of risks and benefits of data-driven medicine and of a learning healthcare system approach;
- Improved communication and understanding between citizens, patients, clinicians, clinical and fundamental researchers, politicians, legal and regulatory authorities, as well as economy:
- A concept that specifies the terms of the patient involvement (e.g., general consent);
- Valid research concepts with stringent verification of big-data-generated hypotheses by other research methods such as randomized controlled trials or mechanistic and analytical basic science methods.

Figure 1: Concept of Precision Medicine.



Source: UKBB, Urs Frey, May 2017.

Similar to many other countries, the availability of large amounts of standardized, health-related, real-world patient and citizen data is still poor in Switzerland. Despite its limited population size, Switzerland can be competitive in the international scientific scene in the field of data-driven medicine due to the quality and the density of the data production in the overall care system. However, this requires the coordination of efforts and design overarching research and healthcare infrastructures. We need to create infrastructures allowing rapidly accessible, consented and ethically approved, fit-for-purpose, interoperable and standardized healthcare data, which can be linked to the available analytical research platforms and biobanks. The latter are heavily developed by our partner organizations ETH with its Personalized Health and Related Technologies (PHRT) initiative, and the SNSF-funded Swiss Biobanking Platform (SBP), the universities, the hospitals and many other health-related research partners (section 4). Together, we aim to establish a reputation as a trusted research partner network.

Personalized medicine will likely transform healthcare in the next decades. Switzerland needs to build a sustainable, personalized medicine ecosystem that delivers a joint venture between citizens, researchers, healthcare providers, authorities and cooperate partners. Dialogue between the relevant stakeholders will be a key instrument for achieving this. SPHN is the first step to facilitating research in this ecosystem.

In order to build up such research infrastructures, the Swiss Federal Government (State Secretariat for Education, Research and Innovation [SERI] and the Federal Office of Public Health [FOPH]) has mandated the Swiss Academy of Medical Sciences (SAMS) and the SIB Swiss Institute of Bioinformatics to build the federal Swiss Personalized Health Network (SPHN) (1). The SAMS and SIB are responsible for the implementation of the mandate, which has been allocated a total of CHF 68 M for the period 2017–2020. A follow-up funding period of the initiative is planned for 2021–2024. After this, the research infrastructures should be self-sustainable.

2. Vision and Mission

With its high-quality healthcare network and excellence in technologies at Universities and ETH Domain Institutions, Switzerland has the potential to become one of the European leaders in health and biomedical science. This enables Switzerland to attract additional national and international funding opportunities and partnerships as well as highly-skilled personnel. To remain internationally competitive and reach this ambitious vision, structural changes in research infrastructural support and changes in data-sharing policies need to be accomplished in the very near future.

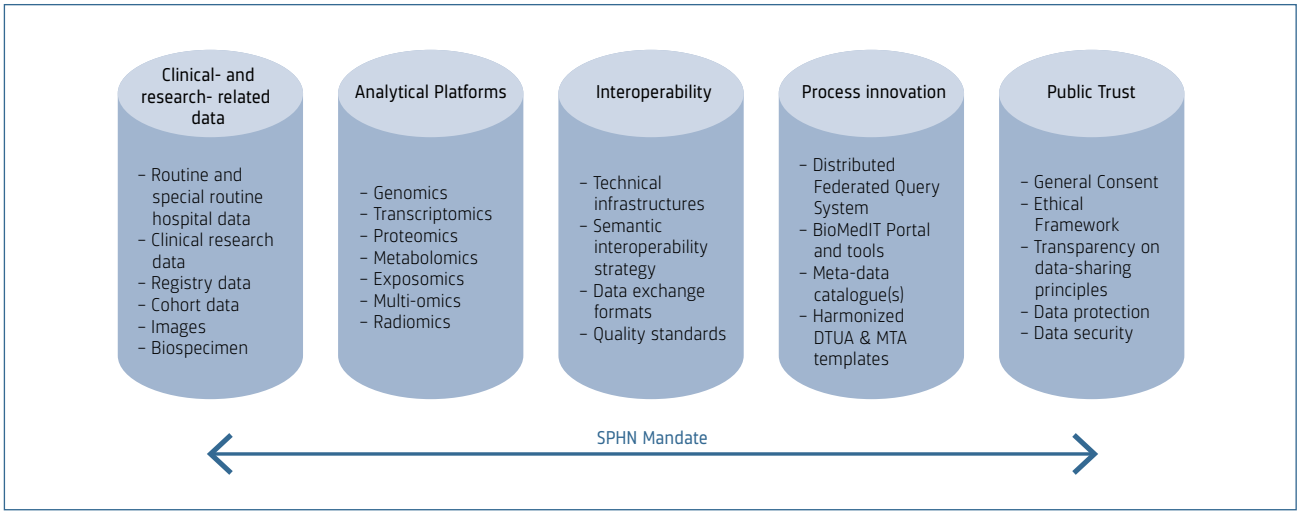
As defined in the mandate, the long-term goal of the SPHN initiative is to establish a Swiss network in personalized medicine, in which all relevant research institutions in this field are involved based on the principles of economy of scale. This implies a stringent coordination of the involved stakeholders and partners. In the period 2017–2020, the central focus is the development of a nationally coordinated research data infrastructure, including interoperability of local and regional information systems in order to optimize the use of primarily clinical but also other health-related data for research in the field of personalized medicine (Figure 2).

A nationally coordinated health-data infrastructure including patient- and citizen-related outcome measures will enable a data-driven precision medicine landscape in Switzerland, leveraging research, industry and care. A data-driven landscape is a transformation instrument that evolves the traditional healthcare system towards a learning, efficient, qualitative and personalized care system. This transformation of the core functioning of the care system will benefit all stakeholders, including governing bodies, public health organizations, the research community and primarily citizens.

We envision a mind shift not only in the medical and scientific community but also in the Swiss public, and a better understanding of risk and benefits of data-driven medicine. We envision the community sharing data in the interest of a better research and clinical-care ecosystem, ultimately in the interest of the patient. We want to achieve this by visualizing SPHN infrastructures, national data streams and multi-omics/multi-source disease- or technology-specific platforms, providing educational tools and connecting partners.

This mind shift also encompasses a real convergence between the initiatives and knowledge held in the research community, and the progression towards interoperability in the healthcare system as enforced by the Federal Swiss Law for the Shared Patient Record. Mutual representatives, such as in the semantic field, ensure that the standards adopted in the massive healthcare system are well-used for the research community. The understanding of the Swiss context – cultural and political – is also an important learning need, notably for the approaches based on distributed architecture. The many stakeholders that have participated in the elaboration of the regulatory aspects of the Swiss Shared Patient Record, law and ordinances, have resulted in a double approach of a centralized, unified layer of services, such as standards, identification and a distributed organization of data.

Figure 2: The Five Pillars of Personalized Health.



3. International Context (ICPerMed, EU-Commission)

Many countries in Europe and overseas have worked on similar initiatives. With notable exceptions, such as the Northern European countries and some Asian countries, most countries face similar problems to Switzerland with poorly interoperable and fragmented healthcare systems. While many international initiatives are often still on a conceptual level and have only recently started to address implementation issues, a clear advantage of the SPHN initiative lies in its combined bottom-up and top-down approach – the SPHN initiative involved researchers and hospitals from its start, and identified practical implementation problems as early as in the first intermediate milestone reports.

Switzerland is involved in the International Consortium for Personalized Medicine (ICPerMed[1]) and maintains close contacts in order to ensure compliance to international standards and interlink at the European level. ICPerMed is a consortium of more than 40 partner countries and regions in the field of personalized health research and infrastructures.

SPHN was involved in the elaboration of the ICPerMed Vision Paper[2] and the mapping of personalized infrastructure mapping efforts in the European research landscape. This will enhance the attractiveness for international research and industry partners, who will likely plan projects in international multi-centre network research consortia. In Section International Review and Gap Analysis from Intermediate Reports, we benchmark the current state of progress of SPHN with respect to the European Union Commission (EC) and ICPerMed Vision and Action Strategy.

The EC will foster personalized health in Horizon 2020 with a focus on implementation. The SPHN initiative will be instrumental to creating a better research environment in order to be competitive for Swiss researchers, in case the 'Swiss-EU-framework agreement'[3] is signed and Swiss researchers can continue to participate in European research consortia via EC-funded RI-projects. However, currently, Switzerland has only an observer status in important EU-research projects such as the 1-Million Genome Project. Switzerland is currently not able to profit from grants provided by ERA-PerMed as no Swiss institution agreed to act as the funding agency.

1 www.icpermed.eu

2 www.icpermed.eu/media/content/Vision_Paper_2019.pdf

3 www.sbfi.admin.ch/dam/sbfi/en/dokumente/2019/02/horizon-europe.pdf.download.pdf/Fact-sheet_Horizon_en.pdf

4. National Context (Partner Organizations)

In the last few years, Switzerland has made significant efforts to foster research and capacity building in personalized health or, more generally speaking, in patient-oriented research. However, many efforts were poorly coordinated. Uncoordinated enthusiasm, poor understanding of the needs of other stakeholders in the complex network, regulatory aspects, financial pressure on hospitals as well as specific stakeholder interests impeded rapid progress of these efforts. During the last two years, the need for alignment and coordination of the efforts became imminent for all stakeholders. SPHN started bilateral talks with PHRT, SNSF, SBP, SCTO, swissethics, unimedsuisse, swissuniversities, eHealth-suisse, patient representatives and many others. Since the beginning of 2019, SPHN and PHRT leadership are meeting and coordinating regularly. The same is true for SBP and SCTO. Representatives of these organizations are invited as observers in each other's Steering Boards. These exchanges have shown their importance for aligning visions, missions and strategic decisions, thus supporting a converging implementation. Shared concerns and challenges are identified and delegated to working groups led by one of the partner organizations, so that the outcome characteristics are usable for all the stakeholders. This process is efficient and also contributes to reinforcing mutual understanding and trust within a national coordination. The need for harmonization was also addressed by the SERI, which officially gave the mandate to the SAMS to coordinate between the stakeholders in November 2019. A subgroup of the SAMS is mandated to elaborate a 'white paper' describing the current landscape of patient- and citizen-oriented health research in Switzerland aiming to develop an overarching, health-related research infrastructure strategy for Switzerland for the next decade.

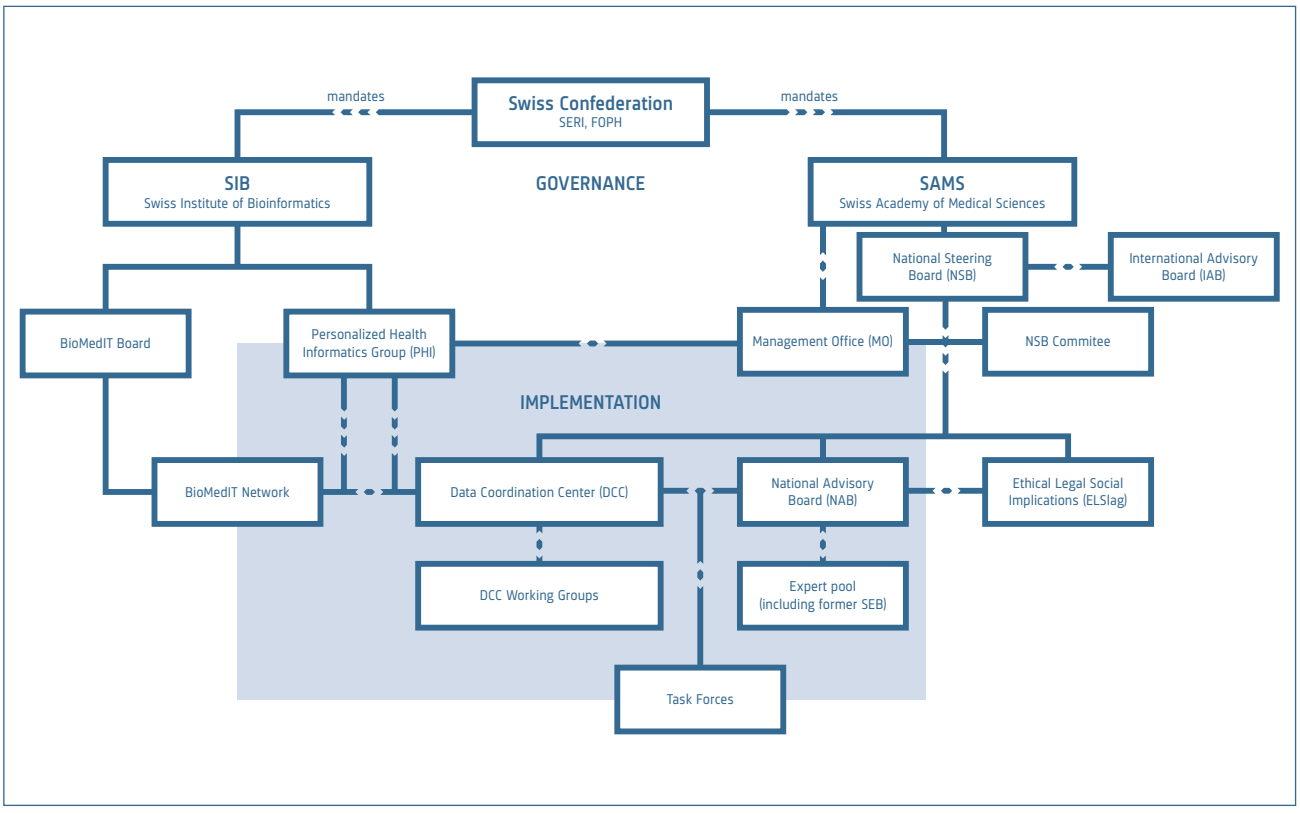
5. Governance and Working Principles of the SPHN Initiative

The SPHN project organization (Figure 3) is characterized by a national governance with several pillars covering the strategic aspects, the scientific and technical elements as well as a strong distributed bottom-up approach with organization and institutions on one side and drivers' projects on the other side (1). Although the Swiss Academy of Medical Sciences (SAMS)[4] is the overarching body of the SPHN initiative, the SIB Swiss Institute of Bioinformatics[5] is responsible for the implementation of the BioMedIT project[6] and the Data Coordination Center[7].

The National Steering Board (NSB)

The National Steering Board (NSB) is the highest body of SPHN and includes representatives from key institutions in Switzerland, notably University Hospitals, Universities, the ETH Domain[8], swissuniversities[9], FOPH[10], SNSF[11] and patient organizations. The NSB is an executive decision-making body: all SPHN strategic and financial decisions are made by this board. It works very closely with the Management Office (MO), which works on an operative level. In addition to the NSB, SPHN is composed of the following Expert Advisory Groups/Bodies.

Figure 3: Organization of Governance and Implementation of SPHN (April 2020).



4 www.sams.ch
5 www.sib.swiss
6 www.sphn.ch/network/projects/biomedit
7 www.sphn.ch/network/projects/data-coordination-center
8 www.ethrat.ch/en
9 www.swissuniversities.ch
10 www.bag.admin.ch/bag/en/home.html
11 www.snf.ch/en/Pages/default.aspx

ELSI Advisory Group (ELSIag)

The Ethical, Legal and Social Implications Advisory Group (ELSIag) addresses ethical, legal and social issues raised with the challenges of personalized health. It is composed of experts from various relevant fields such as bioethics, life sciences legalities and social sciences. ELSIag is the most important place in SPHN, where patients can express their voice.

National Advisory Board (NAB) (formerly Scientific Expert Board)

The SPHN National Advisory Board (NAB) is an answer from the NSB to issues identified during the 2019 SPHN review process identified in the SPHN infrastructure landscape related to the need for a stronger national coordination at infrastructure level.

Being an advisory body, the NAB requires an executive mandate from the NSB to enforce its positions at the decision level. The NAB is composed of a Chairperson and a maximum of 3–5 members covering the following core domains of SPHN:
a) Patient, hospital, and citizen aspects;
b) ICT architecture and interoperability;
c) Analytical technologies (e.g., *omics platforms);
d) Health-data management, life cycle, interoperability, bioinformatics.

The NAB will assemble a group of scientific experts (Expert Pool) with in-depth knowledge of the field of personalized health who are prepared to serve as members of the mandated SPHN working groups. As an advisory body, the NAB has the following duties:
- Infrastructure Roadmap: provide advice on health-research infrastructure development to the National Steering Board (NSB), the Data Coordination Center (DCC) and the BioMedIT Board, similar to the ELSI advisory group's role for ethical aspects of the initiative;
- National SPHN Landscape: examine, review and address issues related to health-research infrastructures and their operations. Contribute to national efforts of harmonization of research infrastructures. Identify and report issues to the NSB, DCC and/or to the BioMedIT Board;
- Gap Analysis: identify gaps and areas requiring action in close collaboration with the SPHN Driver projects, infrastructure providers and working groups of the DCC;
- Mandated SPHN Working Groups: propose mandates for the solving of those issues by bespoke expert working groups. Monitor the establishment, progress and timely elaboration of the mandate deliveries of the working groups;
- International Benchmark: contextualize SPHN efforts within the international landscape. Evaluate new technologies, standards and processes resulting from SPHN projects or international efforts and make recommendations regarding their endorsement and implementation in the SPHN ecosystem.

The International Advisory Board (IAB)

The International Advisory Board (IAB) is composed of international experts in the field of personalized health research. The Board provides advice, expertise and peer-review of funding proposals and of the initiative as a whole.

The Data Coordination Center (DCC) and its working groups

The mandate of the DCC is to promote the development and implementation of nationwide standards for data semantics and exchange mechanisms in order to meet the interoperability goals of the SPHN initiative (Section 6.2).

Working principles of the SPHN initiative

Rather than building a new centralized database, in parallel with the federal landscape for the Swiss Shared Patient record, SPHN adopts a decentralized approach and aims at establishing interoperability of health-related information by building a dynamic scalable and sustainable network of data providers and data recipients based on common standards for formats, semantics, governance and exchange mechanisms.

SPHN supports the development and implementation of coordinated infrastructures by the means of a 5-axis strategy:
- Top-down funding: to develop compatible data management systems in the University Hospitals through Collaboration Agreements (Infrastructure Implementation Projects);
- Bottom-up funding: selection of projects through competitive Calls for Proposals to lead the development of infrastructures and test it with concrete research projects (Infrastructure Development Projects and Driver Projects);
- Secure IT networks: establishment of a secure IT environment (BioMedIT) to support computational biomedical research and clinical bioinformatics without compromising data privacy;
- Mandated working groups: addressing specific gaps, guidelines or coordination tasks;

– Sustainability: by convergence with the running operational processes of the various initiatives held in the Swiss healthcare system.

At the time of the writing of this report, CHF 18.1 M have been allocated to top-down funding projects, CHF 25.3 M to bottom-up projects, CHF 2.6 M to management and CHF 18 M to BioMedIT. The remaining amount of the CHF 68 M allocated by SERI will be used to address identified gaps (Sections 17, 18). Detailed information about the use of funds is available in the Appendix I.

6. Capacity Building

The implementation of the SPHN research infrastructures is of primary interest for patients and healthcare providers as well as for the research community. It is the fundamental basis for the development of novel preventive, diagnostic and therapeutic strategies and measurement of the real-world, data-based value of healthcare in the changing healthcare system driven by the needs of precision medicine and personalized health (Section 20).

Following the finalization of the framing and governance of the initiative, a roadmap to achieving nationwide interoperability of health-related data (2) as well as an Ethical Framework for Responsible Data Processing were defined (3). Upon completion of this groundwork, SPHN initiated its activities in 2017, nevertheless still a considerable amount of work remained to be done (Sections 17, 18). Three years later, the progress made within the framework of the initiative is remarkable: the milestones defined in the Implementation Report of November 2015 (4) have all been met on time and the calls for proposals have even taken place one year ahead of schedule. Numerous working groups and task forces have started their work, and underlying strategies, policies and documents have been developed and published.

6.1. Capacity building in university hospitals: making clinical data shareable

As digital technologies are transforming the health sector, Swiss University Hospitals (UHs) invest a great amount of money in healthcare-compliant ICT infrastructures and processes. In order to streamline and harmonize at least parts of this development and to make health data from UHs sharable and effectively usable for research (i.e., findable, accessible and interoperable), Collaboration Agreements (Infrastructure Implementation Projects) between SPHN and each UH were jointly drafted and signed, with the aim of developing systems that allow interoperable data exchange at all five UHs. To this end, each UH receives a contribution of CHF 3 M over a period of three years, provided that a set of milestones are reached. The development processes at all partner sites are synchronized, following a stepwise implementation approach with staggered milestones grouped in four categories:

- **(A) Consent management and legal framework:** the institutions commit to systematically implementing a process that allows patients to be informed about the possibility of sharing data for research and to making sustained efforts for reaching a significant proportion of inpatients with this information. Furthermore, the hospitals commit to clarifying and documenting their relationship with SPHN with respect to legal framework and procedures that relate to the sharing of consent information and patient data;

- **(B) Definition of Data Interoperability Standards:** the institutions commit to actively contributing to (i) the definition of pseudonymization/coding of data and exchange standards, (ii) the elaboration of a core data set and (iii) the definition of semantics standards enabling interoperability. Furthermore, the institutions commit to establishing and implementing a unique patient ID for research according to the HRA;

- **(C) Development of Clinical Research Data Management Systems**: the institutions commit to establishing an internal IT infrastructure solution (e.g., clinical data management system/clinical data warehouse) for the integration of patient data that can be used for research purposes. Furthermore, they commit to implementing a technical solution regarding the establishment of a federated distributed query system for feasibility studies, allowing researchers to assess if and where clinical data suitable for a specific research question exist at Swiss UHs. Mechanisms for requesting and providing access to distributed data and samples as well as unstructured data will also be developed;

- **(D) Biobanking interoperability:** the institutions commit to implementing mechanisms, allowing interoperability between the biobanking management systems and clinical research data management platforms. This should ensure that sample information can be delivered together with clinical data.

During the first contractual year, all five UHs have actively contributed to developing the legal framework and the procedures that relate to the sharing of consent information and the sharing of patient data. Data sharing is highly critical for the success of the SPHN initiative; access rights may be dependent on the type of data (Section 15).

The implementation of the national harmonized General Consent approved by unimedsuisse[12] and swissethics[13] was deemed as highly desirable.

The UHs are in the process of adopting the standards defined by the Clinical Semantic Interoperability Working Group, such as introducing semantic standards (LOINC, SNOMED-CT), implementing a formal descriptive language for exchanges (RDF) and supporting a strong culture of semantic representation.

The development of the necessary internal clinical research data management systems is well on-track in most UHs. Based on milestone reports, detailed degrees of implementation will be available at the end of 2020. Most of the UH have decided to build platforms that securely integrate, structure and manage health data for further use, including:

– Clinical data (routine data);
– Diagnostic images;
– Anatomic and molecular pathology reports; *omics data;
– Laboratory data;
– Biosample data;
– Patient outcomes.

The internal data management of the UHs is heterogeneous and dependent on the many existing used systems to run their operational activities. However, it generally ends up in a data lake which is made of a federated infrastructure with multimodal, multi-source heterogeneous data. Some of it is secondary centralized, such as what originated from various clinical sources of structured data; some of it remains strongly federated to avoid duplication, such as massive volumes of images.

From this data lake, there are four scenarios of general usage: a) extraction of subsets that are then disconnected from the system. These data can then be sent, for example, to third parties; b) synchronized extraction, for the data sets that remain synchronized with the source data; c) building of an access application programming interface (API) so that third parties' commercial systems used within the hospitals can exploit the data, such as an analytical tool for the management of the hospital or for researchers such as REDcap; and finally some specific development that can directly access the data.

Many of the UHs follow the principle of establishing a data management and analysis platform not only for research but also for patient treatment and hospital operations to best use synergies of a comprehensive analytics platform (5). Concerning Biobanking interoperability, concrete steps are expected in the course of the year 2020.

6.2. SPHN Data Coordination Center (DCC): striving for interoperability, facilitating findability and accessibility

The mandate of the DCC is to promote the development and implementation of nationwide standards for data semantics and exchange mechanisms in order to meet the interoperability goals of the SPHN initiative. For all its assigned tasks, the DCC collaborates closely with its expert working groups. Together:

– they are responsible for the development and technical implementation of a nationwide semantic strategy for clinical data;
– they help define and establish data standards for health-related data, such as routine hospital data, clinical research data, molecular and -omics data and healthy citizen data – in alignment with international efforts;
– they are responsible for the coordination of key milestones of the collaboration agreements between SPHN and the University Hospitals and support the technical implementation of the SPHN infrastructures;
– they coordinate the BioMedIT network and its associated data-providing institutions and ensure technical interoperability among the technical nodes;
– they provide central services to the BioMedIT network in order to streamline processes, enhance security, leverage synergies and foster collaboration.

In addition, the DCC coordinates and aligns the SPHN Driver projects with the infrastructure goals of the initiative and supports cross-institutional collaboration. The DCC operates four working groups (WG), in which various experts of the respective fields and topics are represented. The DCC supports these working groups and ensures coordination and alignment between the groups:

– The **Clinical Data Semantic Interoperability WG** advises on clinical data interoperability standards, data formats and exchange formalisms to be adopted within SPHN (Section 7).

– The **BioMedIT Interoperability WG** develops and implements interoperability between BioMedIT nodes to enable sharing of data and analysis workflows within SPHN.

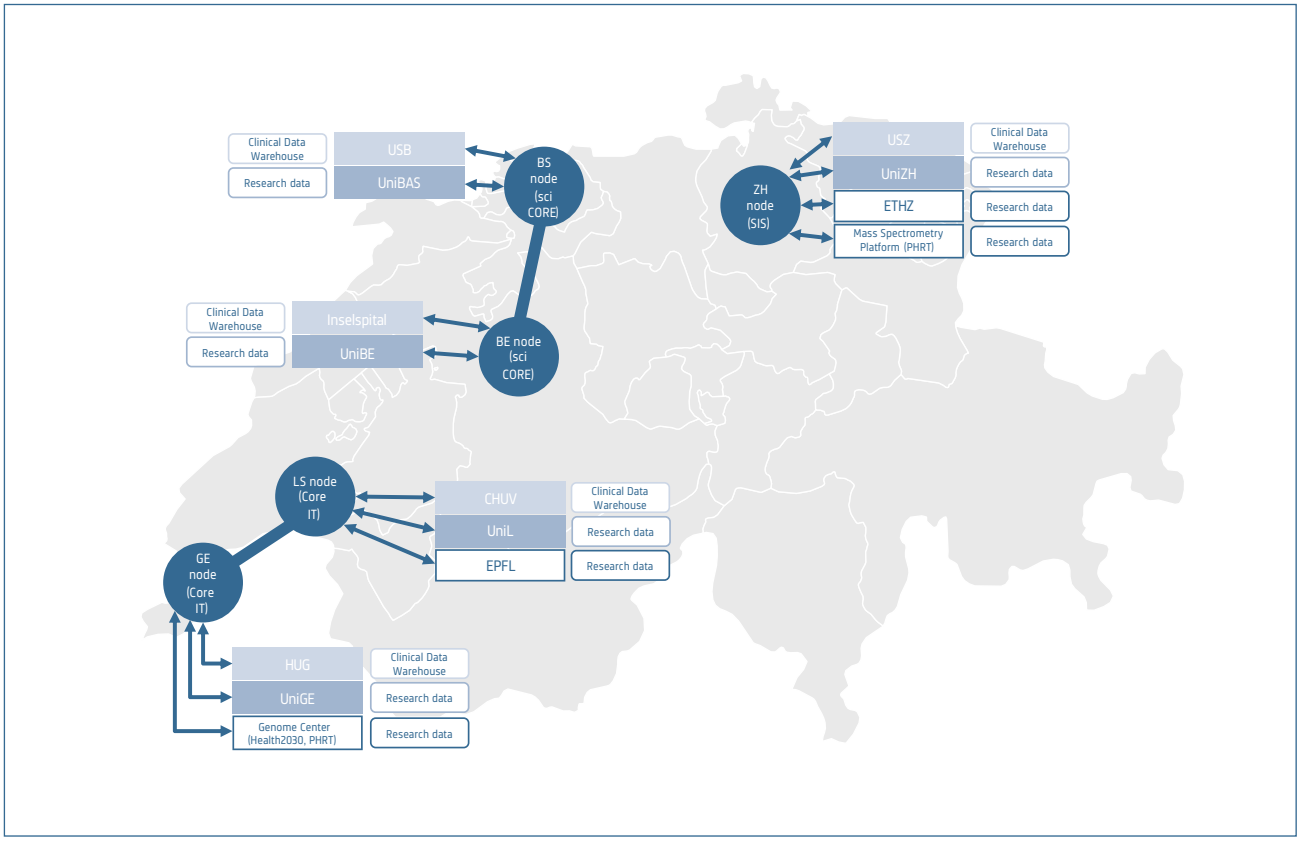
12 www.unimedsuisse.ch/de
13 www.swissethics.ch/en

– The **IT Security WG** advises on security measures for IT infrastructure and for the BioMedIT nodes in SPHN and mitigates security risks through training and awareness.

– The **Hospital IT WG** works towards the identification and prioritization of IT technical needs and a harmonization of processes and IT infrastructures that will ensure interoperability and effective data sharing on a technical level between the UHs. The WG provides recommendations and guidelines regarding the implementation and adoption of technical solutions and standards necessary for the harmonization and development of the Swiss-wide IT infrastructure.

The SPHN DCC is operated by the Personalized Health Informatics Group of the SIB Swiss Institute of Bioinformatics, which is also responsible for the BioMedIT network project (Section 6.3). In addition to the tasks mentioned above, the DCC has a small project portfolio of its own technical implementation projects. The Distributed Federated Query System, supported by the Hospital IT WG, is one of the DCC projects. It allows researchers to run simple queries against a subset of health-related data (core data set) of all University Hospitals, providing information about the number of patients that exist in the system according to the query. This helps researchers to determine the feasibility of conducting a research project and allows research teams from SPHN partners to design, formulate and execute queries across the core data sets provided by the five University Hospitals. Considering the global regulatory aspect of personal data sharing, taking into account the legal umbrella of companies such as the US Patriot Act, the US Cloud Act and the European GDPR, and to ensure the enforcement of the Swiss regulation framework, the DCC identified Clinerion, a Swiss-based company with experience in building networks for querying patient data, as a project partner to help connect core data sets from the five UHs. The system is installed in all five UHs and the first queries are expected to be run in summer 2020. Other projects on the list of the DCC, in collaboration with the Hospital IT WG, are e.g., the development of a national Meta-data catalogue of clinical data, that helps researchers to find out what data in which format would be available for their research. This project is, on the one hand, dependent on the definition of concepts through the Clinical Data Semantic Interoperability WG (Section 7) and, on the other hand, dependent on catalogues of the individual UHs that are currently in preparation. The DCC is also working on a system to streamline data requests: a future data request portal shall point SPHN-accredited researchers directly to

Figure 4: The Swiss Personalized Health Network's Decentralized Approach.



the respective data request portal of the Swiss University Hospital, from which data can be requested. The network is depicted in Figure 4.

6.3. The BioMedIT network

SPHN is committed to investing in interoperability of data and to making data broadly accessible to researchers in Switzerland. In order to leverage the potential of health-related data for better disease prevention, improved medical practice and innovative treatments, it also needs strong capabilities in clinical bioinformatics, computational biology and computational service infrastructure in order to enable the integration and interpretation of large data sets, including e.g., omics or imaging data. The existing computational service infrastructure facilities in Switzerland were not equipped to handle confidential health data, because they were predominantly tailored towards the handling of (insensitive) basic research data.

Given the sensitive nature of health-related information, research using patient data imposes high demands on the Information and Communication Technology (ICT) infrastructures, processes and expertise, in order to fulfil the stringent legal, regulatory and ethical requirements. Security measures for ICT systems are necessary to protect confidential information from unauthorized use, modification, loss or release. Another important requirement concerning the architecture of IT infrastructures for researchers working in multidisciplinary networks on big data sets in the biomedical field is the possibility of shared controlled access to large data sets across research teams from different institutions, and also across borders. In addition, in the context of nationwide collaborative research projects, technical interoperability between different IT infrastructures should be granted, in order to run reproducible data analysis workflows. Packing workflows into containers facilitates bringing the analysis to the data (federated computing), rather than gathering data at the point of analysis. This approach is especially valuable for confidential data or large data sets which cannot easily be shared.

To address the above-listed needs, the BioMedIT network project (Figure 5) was funded by the Swiss federal government for the period of 2017–2020 as part of the Swiss Roadmap for Research Infrastructures within the framework of SPHN and PHRT. The aim of the BioMedIT network is to provide all researchers in Switzerland with access to a service infrastructure for collaborative analysis of confidential data without compromising data privacy. The BioMedIT network builds on three scientific IT services platforms – the BioMedIT nodes – in different geographical locations: one in Basel (sciCORE operated by the University of Basel), one in Lausanne (Core-IT, operated by SIB) and one in Zurich (SIS, operated by ETHZ). Over the past two years, all three nodes established multi-tenant, high-performance storage and compute resources especially for confidential research data that is subject to specific processing conditions.

The BioMedIT network is specifically designed for collaborative research projects on sensitive data that is brought together from different data sources and analyzed by multidisciplinary research teams from different institutions. In the context of SPHN, data generally remains at the site of initial data collection. Data is only copied from different data-providing institutions (e.g., hospitals, universities, technology centres, etc.) to a project space in the context of a specific and approved research project. For project-related data transfer from data-providing institutions, an end-to-end encryption process from the data source through the BioMedIT network to a project space is set up, based on public-key cryptography. Special consideration is given to key management, which is provided as a central service to users of the network. The BioMedIT network follows a hub-and-spoke organizational design (also known as snowflake), in which one BioMedIT node serves as the main (destination) node, on which the data is gathered and processed, while the other two nodes receive the data from data providers in their proximity and route them to the destination node.

The BioMedIT network provides a flexible compute environment and individual project spaces can be configured based on the researcher's computational needs. This includes storage and compute capacities, a configurable tool and software stack as well as backup and archiving means. The nodes can provide work environments for basic exploratory data analysis up to HPC projects such as large-scale machine learning. The network shares a common user identity and researchers can utilize the BioMedIT nodes with a federated login, using SWITCH edu-ID. The BioMedIT portal, a central service of the Network, provides a single-access point to the BioMedIT nodes and associated resources, simplifying access control for the researchers. Depending on the use case, the BioMedIT nodes can be accessed by command-line or by web-based, remote-desktop technology.

The BioMedIT network aims to enable interoperable workflow execution, providing a way for researchers to work seamlessly across the nodes. Containerization of data workflows using Open Container Initiative (OCI) standards are playing an important role for this and will at the same time improve reproducibility of results

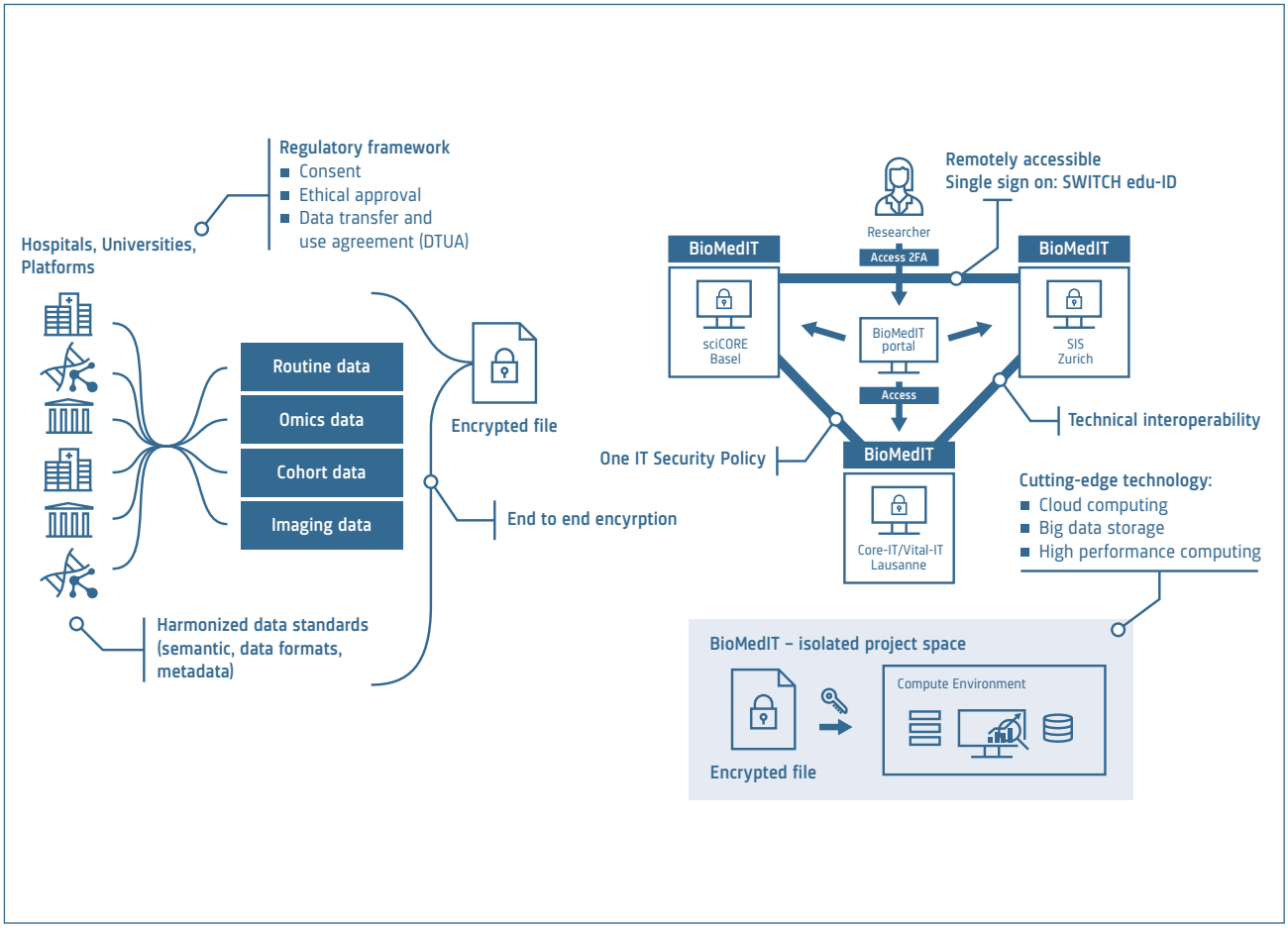
obtained by these workflows. The ultimate goal of the BioMedIT project is to provide a data-aware federated exchange and analysis platform where researchers can work with distributed data. This approach is especially valuable for confidential data or large data sets, which cannot easily be shared.

The intention is to create and maintain a national infrastructure resource that can be jointly used by all Swiss universities, research institutions, hospitals and other interested partners.

The BioMedIT network allows secure and standardized data transfer from data providers to the network, forwarding of data within the network as well as shared controlled access to data sets across research teams from different institutions, while providing cutting-edge technology for data analysis.

The general principle of data handling is based on the FAIR principle (findable, accessible, interoperable, reusable). In a research network, de-identified health-related data can be copied from the individual local nodes and centralized in a safe workspace on this IT platform, where researchers can quality control and analyse the data in a safe, legal-conforming workspace. Alternatively, a network can allow that health data to remain in the hospital environment and research can be done by algorithms travelling to these individual nodes and only report analysed meta-data back to the researcher. Both approaches have their specific advantages and disadvantages: whereas centralized data inherit better options for rigorous quality control, the decentralized approach may be simpler in handling data protection issues.

Figure 5: The Architecture of the BioMedIT network.



7. The SPHN Semantic Interoperability Framework

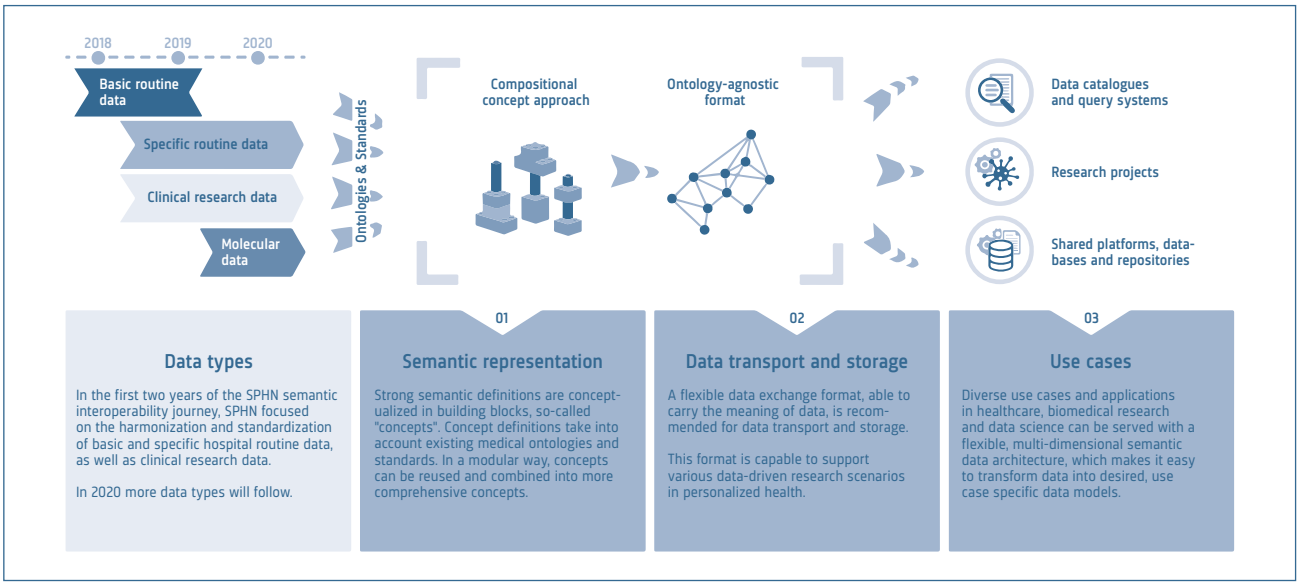
The SPHN Semantic Interoperability Framework (Figure 6) has been elaborated by the Clinical Data Semantic Interoperability Working Group along three axes:

– education and spread of an understanding of the requirements to build interoperability towards shared interpretability of data; data reuse; sustainable metadata framework, such as proposing a central repository for standards;
– building a global data strategy for data interoperability, with three pillars made of semantics; formal descriptive language and data models to bridge with data-use communities such as research, regulatory agencies, public health;
– operational semantic definition of a variety of concepts and the elaboration of a core data set (Section 7.1).

To ensure nationwide interoperability of biomedical data, a variety of issues have to be tackled. The biggest challenge in terms of interoperability is the diversity of data types (Section 15), resulting in an even larger heterogeneity of data standards, data formats, data processing strategies and data quality. Especially with regards to the interpretability of large data sets from different sources, advancing data interoperability is a key success factor. Data interoperability has several layers: semantic, syntactic and technical. SPHN developed a data-driven semantic framework with a strong semantic layer and a model-agnostic flexible technical transport and storage pillar that allows the transport of the data without affecting the semantic meanings.

The question of data formats and clinical data semantics is addressed by the 'SPHN Clinical Data Semantic Interoperability (CSI) Working Group', which faces the challenge of bridging two worlds: the world of healthcare and that of research. The world of healthcare is using and producing large amounts of heterogeneous and multimodal data, such as texts from medical reports, numeric data from laboratory results or images. This is driven by care processes with specific purposes. Building a translational framework allowing the research community to benefit from this large amount of routinely generated data and address research questions in a radically different context requires a strong definition with the objective of conveying meaning and transporting interpretability of data. For example, it is not sufficient to transport the result of a laboratory test. There are several important determinants of the quality and interpretability of the analysis, such as pre-, per- and post-analytical elements. All this information is required to properly interpret the result. To this end, SPHN is developing a data-driven semantic framework with a strong semantic layer and a model-agnostic flexible technical transport and storage pillar, which allows the transport of the data without affecting the semantic meanings. In this way, a semantically driven framework

Figure 6: The SPHN Semantic Interoperability Framework.



Source: NOW Werbeagentur AG, Basel

allows leveraging of the convergence of the data streams and needs in the healthcare system and the data streams and needs of the research community. This convergence will empower a data-driven science approach of the field, in a cooperative and collaborative environment.

7.1. Pillar 1: A strong semantic framework

With regards to languages, there is no effective communication without having a clear and shared understanding of what one speaks about. Whether it is named words, variables or concepts, the most important aspect to enforce is the meaning. Thus, SPHN aims at enforcing a strong semantic definition of data. This is somewhat different from previous initiatives focusing on defining variables as data-type properties, such as string and integer, or acquisition contexts such as date and time.

An important guiding principle is to have this driven by establishing the intersection between what exists (hospitals) and what is needed (research). This list resulting from this intersection is then treated as a list of single elements and concepts that must be, as much as possible, mapped to existing international semantic representations, such as ICD-10, SNOMED or LOINC, or national representations such as CHOP for procedures. This asset of a priori mapped concepts can then be used in the composition of many different research projects.

Concepts are generalizable building blocks, which can be used in different contexts. Each concept contains all necessary information to understand it, and concepts can be combined to compose new concepts in a recursive way.

The list of concepts, their mapping as well as all binding references used to build the mapping to existing semantic sources are available and managed by the DCC.

7.2. Pillar 2: Description formalism for transport and storage

Storage and transport are important challenges. Because data originates in the university hospitals domain, there are constantly new lab analysis, new exam modalities and new structured clinical items. Thus, the data production system precedes the semantic and secondary usage process. It is therefore of prime importance to introduce a storage/transport mechanism that answers the need for plasticity.

Therefore, SPHN aims to implement a data model-agnostic transport and storage approach, such as found in formal descriptive languages. The Resource Description Framework (RDF), already widely used in many domains and in bioinformatics, has been considered as the best choice currently available. By using simple rules, the SPHN clinical data set is used to produce RDF graphs, which contain all data elements. The flexibility of the RDF allows the transferring of national harmonized data, in combination with other data (other standards, format etc.) and allows easy rule-based mapping to existing initiatives. The coverage of the nationally harmonized data set will increase over time; semantic interoperability for data sets containing a large fraction of project specific variables over time is not guaranteed.

7.3. Pillar 3: Model-driven interoperability

There are numerous needs and requirements for existing data exchange in the world, such as OMOP in the research community, CDISC for regulatory authorities such as FDA and FHIR in the HL7 healthcare sector, amongst others. The RDF approach envisioned in SPHN allows the storage/transport layer to be easily bridged to any of these functional-use-driven data models. This strategic approach means that reducing flexibility of the data set representation only is made at the very last step of data transformation, during the exchange process. Data science can be served with a flexible, multi-dimensional semantic data architecture, which makes it easy to transform data into desired, use-case-specific data models.

7.4. Progress 2019

Within the work of the CSI working group, the above-mentioned three-pillar strategy has been developed after a landscape analysis of the different approaches held worldwide, and the challenges encountered. One of the requirements of the SPHN initiative is to support the fundamental and the applied research communities, thus it has to comply to very different needs such as OMOP and CDISC constraints. Driver projects of the first call were approached and their variables collected. Concepts covering the semantics of the variables were prioritized and isolated in an iterative process between the CSI and projects, while developing a better understanding of the semantic constraints. In a first phase, the CSI working group focused on defining the concepts related to variables needed to support the SPHN Driver projects and to fulfil the mandate of the collaboration agreements with the hospitals (published in the SPHN data set V2019.3). Educational workshops, strategic documents, mappings (e.g., strategy-papers, recommendations, guiding documents, releases of the semantic data sets, agreements, etc.) have been produced within this activity area of the SPHN.

8. Capacity Building: Collaboration with Partners and Swiss Multi-Omics Pipeline

In order to test-drive, leverage and develop the SPHN infrastructure further from a clinical research perspective, SPHN teamed up with the ETH Domain. Personalized Health and Related Technologies (PHRT) is a strategic focus area (SFA) of the ETH Domain that started in 2017. The latter embraces key research institutions such as ETHZ, EPFL, PSI, EMPA, Eawag and WSL. PHRT's goals include improving the efficiency and quality of personalized health and precision medicine by providing a range of individual diagnostic and therapeutic strategies for patients.

Through calls for proposals, PHRT funds interdisciplinary projects in education (doctoral and postdoc level), technology translation and interdisciplinary research in order to foster the development of precision medicine and health research. In close collaboration with SPHN, PHRT connects hospitals and the institutions that constitute the ETH Domain so that they can commonly share, analyse, exploit and use health data across Switzerland. The two programs complement each other and coordinate their activities in order to promote personalized health and personalized medicine in Switzerland.

Besides the SPHN, the PHRT program is complementary to and operates in close cooperation with other programs in Switzerland, in particular, the Swiss Data Science Center (SDSC) (another ETH Domain SFA), the Health 2030 initiative and the Personalized Health Alliance Zürich-Basel. In addition, it is linked to international research efforts, including "The Cancer Genome Atlas" (TCGA), the "Cancer Moonshot" initiative, both at the National Institutes of Health (NIH, USA) and the Global Alliance for Genomics and Health (GA4GH).

The main objective of PHRT is to provide the ETH Domain know-how to support and improve clinical decision-making for the benefit of (Swiss) patients. This know-how currently includes various worldwide unique types of molecular measurements and the capacity to analyse multi-dimensional data sets within the clinical context with innovative bioinformatics and next-generation data-analysis strategies.

In order to build up clinical research data generation and clinical data analysis capacity, PHRT has established three centres in Switzerland enabling the molecular digitization of large clinical sample cohorts. These centres, as the basis of a Swiss multi-omics pipeline, can generate and analyse data in a coordinated fashion from the same clinical biospecimen on the genomic, transcriptomic and proteotype level:

- **Clinical Genomics Analysis Center**
  The Health 2030 Genome Center, based in Geneva, aims to provide answers to the large-scale sequencing needs of Switzerland and to integrate and synergize with several groups working on human genetics and genomics, thereby facilitating genomic research and the implementation of genomic-based medicine;

- **Clinical Proteotype Analysis Center**
  The Clinical Proteotype Analysis Center in Zurich is a comprehensive and coordinated effort to accelerate the understanding of the molecular basis of disease/wellness, through the development and application of robust and quantitative mass-spectrometry-based strategies;

- **Clinical Metabolome Analysis Center**
  The newly created centre in Zurich aims at analysing the metabolome and assessing its impact on the understanding of the mechanisms of diseases.

This Swiss multi-omics pipeline is directly connected via the DCC to hospital-based data warehouses, allowing safe interoperability between basic science and clinical science. The key challenges which are being addressed by PHRT and the two centres are:

- to improve the performance (robustness, sensitivity, reproducibility, etc) of ETH Domain technologies to a level sufficient to support and contribute to clinical decision-making and compliance to the regulatory framework;
- to evaluate different data levels being generated by individual and combined ETH Domain technologies for their potential to support clinical decision-making:
  - level 1 data refers to data which is of direct clinical relevance within the current standard of care (0.1% of the data);
  - level 2 data refers to data for which clinical evidence exists supporting likely clinical benefit beyond standard of care (less than 10% of the data);
  - level 3 data refers to the vast majority of data, which is potentially relevant, but for which no conclusive data is available (more than 90% of the data);

– to make the raw and meta-data available for further research leading to new knowledge beyond institutions of the ETH Domain, and the development of next-generation analysis strategies as an education, invention and innovation engine together with Swiss hospitals;
– to collect and evaluate suitable biomaterial for the technologies available and getting access to biobanks;
– to (further) develop ETH Domain technologies to contribute to personalized health and precision medicine.

This close coordination of SPHN with PHRT in the context of infrastructure building led recently to a national strategy of a federated genomics and metabolomics/proteomics network which is currently elaborated in mandated SPHN working groups (Section Mandated scientific SPHN working groups).

9. Process Innovation, Codes of Conduct: Adapting Procedures and Frameworks to New Developments

The infrastructure developed by SPHN aims to enable and facilitate research in the field of patient-oriented research and particularly personalized medicine. Infrastructure is meant at large by covering governance, education, standardization of semantics, exchange format and tools, technical infrastructures and processes, including all that pertains to data management, ethical boards, consent and recognition of contributions. Advisory and expert groups within SPHN, but also partner organizations, such as SBP or unimedsuisse, elaborated various documents addressing process innovation or standardization. These processes cover a broad range of areas e.g., technical, regulatory, ethical and legal domains (Table 1).

For example, the Ethical Framework is one of the core documents of SPHN and provides ethical guidance to the partners of the network with respect to the collection, storage, analysis and sharing of personal data for research purposes. As health-related personal data are often derived from human biological material, both data and human biological material are addressed in the framework. With the Data Transfer and Use Agreement (DTUA) template, a harmonization of the legal processes related to the transfer and use of data between Swiss research institutions and University Hospitals was achieved. Researchers now have a template that is common to 15 institutions facilitating the contracting process between big research consortia.

Of note, many of these guidelines and recommendations have been established by multi-stakeholder working groups including patient representatives. These documents are a significant step towards a common understanding of health-research data-related processes in Switzerland. Many of them are still on a conceptual level. They now face real-life implementation testing in the various Driver projects. These documents should be considered as living documents: these first versions are a first step. These recommendations are significantly better than the previous heterogeneous federal regulations. However, during the implementation process it is expected that more advanced versions will evolve within the next few years. These recommendations must remain supportive in nature for the researchers. Interoperability of data within the federated health and research system is critically dependent on a common understanding of researchers, clinicians and citizens. These stakeholder groups need to agree that nationally harmonized regulatory frameworks are critical for the progress of patient-oriented research and healthcare progress in Switzerland.

Table 1: SPHN's contributions to process innovation.

Ethical-legal-social implications (ELSI)	Technical
Ethical Framework (including data-sharing principles)	Infrastructure Roadmap (BioMedIT network)
Guidance on the Return of Actionable Clinical Findings	IT Information Security Policy (DCC/SIB)
Data Transfer and Use Agreement (Template)	Data Semantic Interoperability Strategy (DCC)
Material Transfer Agreements (Template) (Swiss Biobanking Platform)	Hospital IT Strategy (DCC)
General Consent (unimedsuisse, swissethics, SAMS)	Distributed federated query system (exp. 2020, DCC/SIB, Hospital IT)
SPHN Glossary	

10. Infrastructure Establishment Throughout the Country: Driver and Infrastructure Development Projects

SPHN launched two calls for proposals (in 2017 and 2018). The primary aim of SPHN is the development of sustainable research infrastructures. SPHN is not a classical research funding body. Nevertheless, in real life, research infrastructures cannot be built up independently of research projects. Thus, two types of funding schemes were developed:

– **Infrastructure Development Projects** developing and testing new technologies, methods and infrastructures at single or joint sites, to be made available to other institutions after proof of concept and;

– **Driver Projects** guiding the development of SPHN by test-driving the infrastructures and interoperability for multi-site research in a specific area or pathology. Each Driver project typically involves multiple data providers (predominantly University Hospitals, but also universities and analytic platforms) as well as teams of data recipients, who analyse the data, which is securely transferred from the data providers to the data recipients via the BioMedIT network.

Both calls were open regarding topics and areas of research. In the second call, priority was given to projects that address the following gaps, which were identified after the first round of project selection: i) imaging and radiology interoperability, ii) public health and healthy citizens and iii) nationwide interoperability of cohorts and registries. The two calls were closely coordinated with PHRT.

Selected from an overall of 76 proposals requesting CHF 90.4 M, SPHN funded 24 projects (incl. 6 co-funded by PHRT) (Table 2, Table 3). In addition, SPHN financed 5 Infrastructure Implementation Projects at the University Hospitals (CHF 15 M). As an integral part of SPHN, SERI also funded the BioMedIT project at SIB (CHF 18 M). To date, CHF 58.3 M was invested into research infrastructure projects. A lay-summary of each project is available on the SPHN website (sphn.ch).

The first annual activity and financial reports of the projects awarded in 2017 were submitted on 31 March 2019. The review of the first activity reports revealed that the projects are in general on-track with respect to infrastructure development, with a good amount of the proposed infrastructure milestones being met. Self-reported degree of implementation of the various research infrastructures was assessed in the intermediate milestone reports. The degree of implementation of research infrastructures was classified as follows:

1. Concept established;
2. Infrastructure built and tested;
3. First scientific study successfully performed on the described infrastructure;
4. Infrastructure tested with multiple studies;
5. Infrastructure available for projects outside the project consortium;
6. Infrastructure used for clinical diagnostic or therapeutic applications.

The main project deliverables and the mean degree of infrastructure implementation (self-reported values Spring 2018, Table 2, Table 3) are available for projects which started in 2017.

Table 2: Infrastructure Development Projects Awarded in 2017 and 2018.

Project title	Main project deliverable	Average degree of implementation[14]
E-General-Consent: Development and Implementation of a Nationwide Harmonized Interactive Electronic General Consent Prof. Christiane Pauli-Magnus, Basel	An interoperable professional grade, electronic general consent solution.	3.67
Development of a Governance and Quality Management System for Exchange of Patient Related Data for Research Purposes Dr. Joerg Willers, Basel	Development and implementation of tools (e.g., rules and regulations, generic sets of templates) for data governance at an institutional level that allow controlled and secure handling of sensitive data.	Not available
C3-STuDY: Citizen Centered Consent: Shared, Transparent and Dynamic Prof. Christian Lovis, Genève	Technical backbone infrastructure of a structured and computerized consent, which can be shared, is transparent, dynamic and interoperable, in the form of a personalized communication platform around research.	4.75
DeID: De-identification of Clinical Narrative Data in French, German and Italian Prof. Christian Lovis, Genève	A rule-based de-identification system to process free-text medical data in French, German and Italian for secondary usage.	3
Harmonising the Collection of Health-Related Data and Biospecimens in Paediatric Hospitals Throughout Switzerland Prof. Claudia Kuehni, Bern	Inventory of all health-related data collected from children in Switzerland, consensus on the hospital core data and biosamples to be collected, knowledge whether parents are willing to provide health-related information via paper questionnaires, web-based or mobile phone apps.	1
LOINC for Swiss Laboratories (L4CHLAB) Prof. Christian Lovis, Genève	List of interoperable LOINC codes for usual laboratory analysis.	5
Swiss Variant Interpretation Platform for Oncology (SVIP-O) Dr. Daniel Stekhoven, Zürich	Curated database for the harmonized, clinical interpretation of somatic variants identified in cancer patients from routine diagnostics in Swiss hospitals.	1.67
NLP-Powered Mapping of Clinical Reports onto SNOMED-CT Concepts for Tumour Classification (NLPforTC) Dr. Thomas Fabbro, Basel	Implementation and evaluation of a NLP-driven process to map information from radiology and pathology reports related to tumour onto the SNOMED-CT terminology. Based on the extracted information, a Tumour-Node-Metastasis (TNM) classifier will be developed in order to predict the tumour class of individual patients.	3
SwissGenVar: A Platform for Clinical Grade Interpretation of Genetic Variants to Foster Personalized Healthcare in Switzerland Prof. Anita Rauch, Schlieren	IT-infrastructure and application working as a knowledge-sharing platform to provide standardized interpretation clues and expert discussions on individual variants and to facilitate consented high-quality data sharing for personalized health research.	Not available
SwissPKcdw: Optimising Paediatric Dosing Regimens Based on a cCinical Data Warehouse§ Prof. Christoph Berger, Zürich	A Swiss PharmacoKinetics Clinical Data Warehouse and an online platform SwissPKcdw with focus on paediatric pharmacokinetics in order to optimise dosage regimen for children.	Not available
Swiss BioRef: Personalized reference values for precision medicine§ PD Dr. Alexander Leichtle, Bern	Infrastructure to generate and provide more accurate reference ranges for the Swiss population, based on laboratory data from hospitals and study cohorts.	Not available
MedCo: Enabling the Secure and Privacy-Preselving Exploration of Distributed Clinical and -Omics Cohorts in SPHN* Nicolas Rosat, Lausanne	A production-ready and hospital-compliant version of the current academic MedCo prototype, which can be deployed and used in the Swiss Personalized Health Network.	Not available
QA4IQI: Quality Assessment for Interoperable Quantitative CT-Imaging* Dr. Bram Stieltjes, Basel	Infrastructure for integrating imaging data in research in personalized health and translating advanced image computing techniques to clinical practice.	Not available

§ These projects were submitted as Driver projects but are funded as Infrastructure development projects.

* Co-financed by SPHN and PHRT (ETH-Domain). The figures indicate the amount received from SPHN only.

14 Self-reported values (Spring 2018).

Table 3: Driver Projects Awarded in 2017 and 2018

Project title	Main project deliverable	Average degree of implementation[15]
Swiss Frailty Network and Repository (SFNR) Prof. Heike Bischoff-Ferrari, Zürich	Swiss consensus on how to assess frailty clinically within the comprehensive Geriatric Assessment. Definition of an eFrailty-Index and establishment of a shared data bank.	1.67
Population-Wide Screens of the Human Immune Repertoire Prof. Adriano Aguzzi, Zürich	Establishment of a data infrastructure, allowing high-throughput screening campaigns with relevant antigens to identify the immune profile in very large cohorts, data analysis and correlation with clinical information of patients to detect biomarkers in health and disease.	2.33
Swiss Molecular Pathology Breakthrough Platform (SOCIBP) Prof. Mark Rubin, Bern	Breakthrough genomics platform to manage and share oncology data across Switzerland using a uniform genomics language.	3.17
Swiss Personalized Oncology (SPO) Prof. Olivier Michiélin, Lausanne Prof. Mohamed Bentires-Alj, Basel	1. Data warehouse infrastructure for data capture from University Hospitals and web-based system for non-university cancer clinics; 2. National molecular tumour board with expert panel; 3. Standardized molecular profiling procedures of tumour biopsies.	1
Identification of Biomarkers and Therapeutic Targets in Inflammatory Disease Immunotherapy by High-Dimensional Single Cell Analysis and Cluster Proteomics Prof. Manfred Claassen, Zürich	1. Cell identity biomarker for therapy response in Multiple and Systemic Sclerosis and Psoriasis; 2. Interoperable data resource of clinical & molecular data for Swiss wide immune disorder patient cohorts; 3. Transferrable cell population biomarker discovery pipeline (installed at facility infrastructure UZH/ETHZ).	1.5
Personalized Swiss Sepsis Study (PSSS) PD Dr. Adrian Egli, Basel	Interoperable infrastructure among the intensive care units of the Swiss University Hospitals and several research groups, to gather complex information on the host and pathogen during the entire course of a sepsis.	3.5
SACR: The Swiss Ageing Citizen Reference Prof. Nicole Probst-Hensch, Basel	The Swiss Ageing Citizen Reference will make existing data and biospecimens from 1000 deeply and longitudinally characterized citizens (SAPALDIA, CoLaus/PsyCoLaus, SKIPOGH) accessible to personalized health researchers.	Not available
CREATE PRIMA: Clinical Research From Multi-Modality Big Data Sources Without Proprietary Interfaces in a Multi-centre Approach Prof. Jörg Leuppi, Basel	The CREATE system is an innovative approach to the management of complex, unstructured data. The project will enable interoperability between systems and organizations and exchange of nationwide routine clinical data.	Not available
IMAGINE: Radiomics for Comprehensive Patient and Disease Phenotyping in Personalized Health Prof. Matthias Guckenberger, Zürich	Swiss-wide infrastructure for image-based biomarker research & analysis. Development of standardized imaging, image analysis and image-based outcome modelling to evaluate the value of MR images acquired in clinical routine as prognostic and predictive biomarker in patients treated for Glioblastoma multiforme.	Not available
SOIN: Swiss Ophthalmic Imaging Network Prof. Thomas Wolfensberger, Lausanne	A secure, integrated image and data capture, management and analysis platform for ophthalmology in Switzerland. Development, testing and refining of a predictive AI software tool for optimizing personalized protocols for the timely delivery of treatment (anti-VEGF injections) in AMD.	Not available
SHFN: SWISSHEART Failure Network Prof. Christian Matter, Zürich	A standardized data infrastructure for a SwissHeart Failure Registry, which will collect clinical, laboratory, electrocardiogram and imaging data of patients at risk for HF (patients with heart attack) and patients hospitalized for acute HF.	Not available

* Co-financed by SPHN and PHRT (ETH-Domain). The figures indicate the amount received from SPHN only..

15 Self-reported values (Spring 2018).

11. Mapping of Activities: Where Do We Stand?

Taking advantage of the annual reports, the SPHN-funded projects were requested to provide information on infrastructure built in 2018 and 2019 in a structured way, determining the research orientation of their project (patient- or citizen-oriented; ethics, legal domain, data protection, patient information; analytical platforms (e.g., genomics, metabolomics, etc.); bioinformatics, medical informatics, big data analytic platforms; national registries, technology and analytical networks) as well as the degree of implementation (Section Infrastructure establishment Throughout the Country: Driver and Infrastructure Development Projects). This information was used to create an initial mapping and to start a gap analysis.

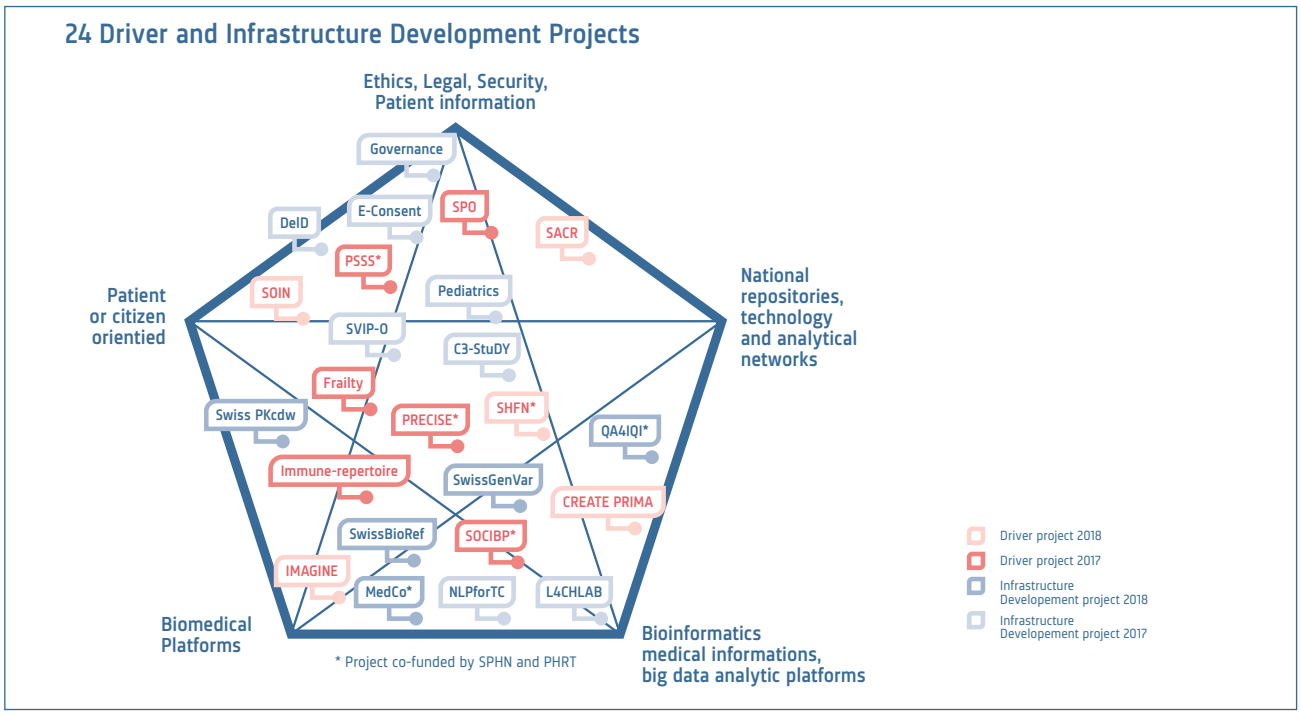
The mapping shows that many domains are covered by the projects, however, it seems that more activities in the "patient- or citizen-oriented" and "national repositories, technology and analytical networks" domains might be needed (Table 4, Figure 7).

Table 4: Overview of Newly Built Infrastructures During the First Two Reporting Years (2018 & 2019).

	2018			2019		
	Infra. Dev. projects	Driver Projects	Overall	Infra. Dev. projects	Driver Projects	Overall
# of projects	7	6	13	12*	11	23
# of newly built infrastructures	24	18	42	36	35	71
Average degree of implementation	2.6	2.1	2.4	2.9	2.2	2.6
Median degree of implementation	2	2	2	3	2	2
Highest degree of implementation	5	4	5	6	4.5	6

* One Infrastructure Development Project was not included as the information was not yet available.

Figure 7: Driver and Infrastructure Development Projects of SPHN Mapped According to Their Research Orientations.



Source: NOW Werbeagentur AG, Basel

12. Ethical, Legal and Societal Aspects

The initiative compares various ethical, legal and societal challenges arising with regard to its activities, which are addressed by the ELSI advisory group. Since 2017, the ELSI advisory group has issued ethical guidance on responsible data processing, data transfer and use and reporting of actionable genetic findings to research participants.

The "Ethical Framework for Responsible Data Processing in Personalized Health Research" provides ethical guidance to the partners of the Network as to the collection, storage, analysis and sharing of personal data for research purposes. The framework puts forward four ethical principles: respect for persons, privacy, data fairness and accountability. These principles should guide the conduct of researchers and the activities of institutions that participate in SPHN when processing personal data or handling human biological material, in particular with a view to sharing such data and material within SPHN. Each principle is followed by a set of specific guidelines intended to assist participating institutions to abide by the principles.

The document "Reporting Actionable Genetic Findings to Research Participants" contains recommendations to ensure ethically responsible handling of genetic research findings that have potential medical relevance for individual research participants involved in SPHN-funded studies. The aim of these recommendations is to raise awareness in SPHN grantees about the medical and ethical importance of defining a clear strategy for reporting of research findings to research participants. At the same time, they offer concrete indications about how to meet the ethical obligations of researchers towards research participants. Adherence to the recommendations presented here will promote more harmonized and accountable decisions in this ethically sensitive issue and will increase public trust in SPHN as well as in SPHN grantees.

Additionally, SPHN and Swiss Biobanking Platform have worked in close collaboration to develop the "Data Transfer and Use Agreement (DTUA)" and "Material Transfer Agreement (MTA)" templates to facilitate data and material exchange in the context of academic research projects. The templates define rights, responsibilities and obligations of involved parties (e.g., provider, recipient, processor) regarding permitted use, ownership, publications, intellectual property and liability when data is being transferred or accessed in the frame of a project. While each institution has been using their specific DTU agreement, the DTUA template is part of a national harmonization effort. SPHN and SBP encourage their partners as well as anyone working with data or biological material in Switzerland to adopt these templates.

Lastly, the ELSIag has developed a Glossary in order to ensure that SPHN stakeholders, partners and participating institutions share a common understanding on the most frequently used legal and technical terms related to SPHN.

13. Data Protection Aspects

According to the Swiss data protection law and European General Data Protection Regulation (GDPR), the key elements ensuring data protection are appropriate safety measures, availability of codes of conduct and accountability of the researchers. Working within SPHN infrastructures supports aspects of data safety (Section 6.3, Section 13) as well as recommendations in respect to biobanking elaborated by the Swiss Biobanking Platform[16]. Codes of conduct are supported by the general consent, ethical framework agreement, the recommendations for return of actionable findings (Section 12) and various other standard operating procedures. The data protection aspects of the program are elaborated in close cooperation with the Swiss Data Protection Officer.

14. Patient Involvement

Patients have rights with respect to data protection. However, they also have the right and interest that research can be achieved to improve healthcare or advance knowledge in their specific disease. There is a delicate balance between these two interests. Patients need to be involved in the processes and are important stakeholders. The dialogue with patients and the building-up of trust are key pillars for successful research in personalized health. Identifying representative patient groups and creating dialogue channels is not trivial. Not only SPHN, but also the SCTO and SBP have interests in building up structures which enhance patient involvement. In a joint effort, a working group led by the SCTO in close collaboration with patient organizations (bottom-up approach) aims to create a map of research-related patient and citizen involvement and empowerment activities in Switzerland. By creating a Swiss Patient and Citizen Involvement Think Tank for Personalized Health and Clinical Research, the related needs of these patients will be identified.

16 www.swissbiobanking.ch

15. Data Structures and Use Cases

15.1. Availability of clinical data in the hospital environment for research purposes

The use of clinical data for research purposes is one of the most critical issues of the SPHN initiative. There is an increasing awareness of data ownership, data protection, and ethical and legal issues related to the secondary use of health-related data involving patient-oriented but also citizen health data. Many of the aspects have been addressed by the SPHN initiative and important process documents have been agreed on in order to facilitate the ethically and legally compliant transfer and secondary use of data. The mode of data access, data aggregation, data processing and data storage will be very heterogeneous and will depend on the type of data including its associated features (e.g., degree of quality, consent status, degree of structuring, etc.) as well as the research question or the use case. In parallel, there is increasing pressure from the research community including industry partners to have access to clinical data in order to remain internationally competitive in patient-oriented research, but also to be attractive as partners for the biomedical research industry. This will also be instrumental for the national economic situation.

In order to clarify the situation, we aimed to characterize different categories of data types as well as use cases. The latter will be helpful for a more focused discussion on, for instance, handling access rights, intellectual property (IP) issues and standard operating procedures (SOPs).

15.2. Type of patient- and citizen-oriented health data available for research

In the last decade, Swiss patient- and citizen-oriented research has been known for its high quality, structured cohort and registry data. Furthermore, clinical scientists maintain registries for specific disease entities in a nationally or internationally standardized manner. Such structured data are similarly useful for SPHN-related research; interestingly enough a significant number of SPHN Driver projects are based on structured or cohort data. However, the governance, the consent situation and the data-sharing principles for such structured data may be different from the principles needed for unstructured hospital data generated after general consent has been given. It has been suggested that the governance, the ethical and legal aspects and the data-sharing principles may have to be defined with respect to the type of health-related data and the research question (use case).

We therefore aimed at characterizing different health-related research data based on the following criteria:

i. Type of data;
i. Original purpose;
ii. Degree of processing;
iii. Degree of structuring;
iv. Quality control;
v. Data protection status;
vi. Return of actionable findings;
vii. Data governance and ethics requirements;
viii. Related research stakeholders;
ix. Utility for PH Research, utility for clinical research;
x. IP scenario recommendation.

Depending on the initial clinical or research purpose of the health-data collection, and dependent on the degree of structuring and quality motivated pre-processing, data sets can be grouped into different categories, ranging from clinical data extracted from clinical information systems into a data lake, specific routine data, molecular or -omics data to citizen/consumer health data (see Appendix II: Data Types).

Finally, for each data type, examples of SPHN and PHRT projects are presented (where applicable). The further use of these data will depend on the above-mentioned criteria and needs to be defined for each category (Appendix II, Table 10).

Such categorization may be helpful to better define SOPs and recommendations for the secondary use of such data for research, accounting for the specific ethical, legal and governance aspects. It may also help to increase the willingness of involved stakeholders to share data for further research and may enhance new collaborations with existing consortia of clinician scientists. For example, unstructured hospital data, which is generated in an automated manner can easily be shared for research purposes. However, it is unlikely that a consortium of clinical or basic scientists, who have invested time, money and careers into quality control and structuring of data, will share data without participating as collaborative research partners. In real life, such situations have to realistically be considered. It is important to catalyse the involvement of all relevant stakeholders in the projects.

15.3. Scientific 'use cases' to guide future research projects

SPHN is a research infrastructure development initiative. It aims to build up infrastructures and processes that will allow future researchers to overcome hurdles which are typical challenges for personalized health and related research, or even patient-oriented research in general. We defined a series of use cases exemplifying these challenges based on knowledge derived from the SPHN and PHRT Driver projects.

SPHN and PHRT aim at facilitating the handling of these typical 'research use cases' by visualizing SOPs and training tools useful for the future researchers (Section 16).

The use cases can be grouped into the following main categories and typical research questions:

- **Category 1:** Molecular and digital biomarker and multidimensional signatures discovery – personalized prevention, risk identification and better/earlier diagnosis, prediction of outcomes, treatment and intervention strategies as well as clinical decision support in specific disease entities.

- **Category 2:** Data-based hypothesis generation – discovery of medically relevant associations, early signals and changes of disease trajectories in order to improve safety and quality of care after validation of the hypothesis in clinical studies or to improve discovery of associations to support the subsequent analytic testing of related biological mechanisms and basic science.

- **Category 3**: Patient identification for further targeted research projects – identification or improvement of health data sets e.g., for clinical trials or rare diseases, identification of drug targets, more expansive interoperable health records should make it easier to find suitable participants for observational or interventional studies (RCTs).

- **Category 4**: Reference cohorts/data sets – establishment of large-scale population cohorts/data sets in order to be able to control for biological variations (e.g., genetic variants, reference ranges for laboratory values).

- **Category 5**: Drug targeting and drug efficacy – enhancing therapeutic treatment, assessment of real-life PK-PD relationship and drug effectiveness or earlier detection of drug side effects, drug efficacy in specific patient subgroups.

- **Category 6**: Process improvement – establishment of tools or decision platforms to improve, digitalize or simplify processes in the healthcare setting (e.g., scalable data curation tools, high-throughput image processing and quality control, automatically generated reports and report annotations).

- **Category 7:** Quality improvement of patient and citizen healthcare (Health Services Research) – comparison of interventions to those recommended by guidelines, assessment of quality of life, societal and health economic aspects of prevention and care, lifestyle, societal and environmental impact (exposomics) on health, health economic aspects as well as patient guidelines, regulatory aspects.

- **Category 8:** Development of mobile health applications or medical devices – establishment of new technical solutions for data sources, complementary to already existing data sources. (e.g., apps for patient self-reporting or to test cognitive skills).

These use case categories were structured in terms of their use and need of research and clinical infrastructure as well as required regulatory documents and processes. These are: the need for a data query system, the availability of biobanks, the need for multi-omics analytical platforms, IT infrastructures and big data bioinformatics, IT-cloud technology, data governance, consent status, ethics requirements, SOPs, regulatory aspects, IP aspects and potential clinical or scientific impact. A large number of Driver projects fit in Category 1 and Category 2, however, most categories were represented in at least one Driver project. Unfortunately, health economics and mobile device use cases are missing from the current SPHN portfolio.

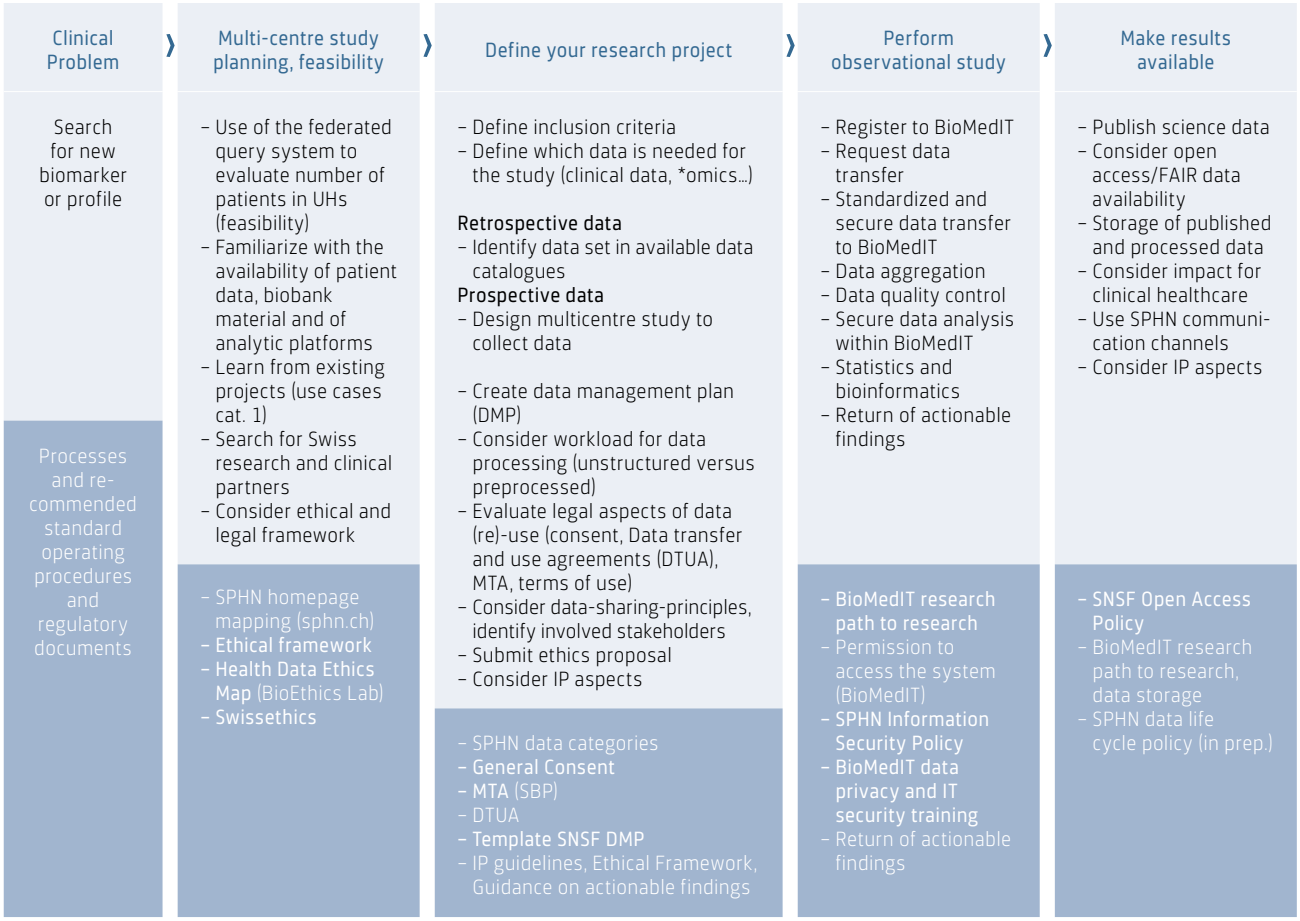
16. Mapping and Visualization

The major hurdles of big data health science in Switzerland are the complexity of data influencing health as well as the heterogeneity of the health system. Moreover, the Swiss research governance organizations take time to understand and address the true problems. Successful countries, in contrary, have a centralized coordination for semantics, standards and processes. On the other hand, however, the beauty of health-related research in Switzerland is the high quality of the data and the enormous potential of technical innovation and analytical platforms. In order to boost personalized health in Switzerland, the improvement and dissemination of knowledge about available infrastructures, data sets and SOPs are key. It will help future researchers to learn from experienced consortia having dealt with a specific use case, and to find new research partners in Switzerland. The considerations below are targets SPHN wants to achieve in the next few months and years. It is currently a work in progress.

16.1. Finding research partners, support structures, data and research consortia

SPHN has set up a new interactive webpage[17] for researchers, clinicians, citizens and funders. It maps hospitals, research institutions, health databases and registries, analytical platforms, quality and security standards, ongoing research and infrastructure development projects in Switzerland and national and international research consortia but also regulatory, ethics and legal documents necessary for health-data-related research in Switzer-

Figure 8: Visualising Use Case Category 1: Biomarker and Multi-Dimensional Signatures Discovery.



17 www.sphn.ch

land. In the specific pages dedicated to the lay public, it contains links to resources explaining the utility, benefits and risks of personalized health research.

The webpage addresses frequently asked questions and refers to other institutions if related items are not in the mandate of SPHN. The page is stringently interlinked with the websites of e.g., SBP or SCTO, and directly refers to available biobanks and regulatory and legal documents needed to deal with biospecimens. The webpage is similarly strongly linked to the PHRT webpage, helping to find analytical platforms and new research-related technologies. The new SPHN webpage will particularly help young researchers to find new research partners, funding, process support and last but not least access to health-related data and analytical platforms.

16.2. Use-case approach to personalized-health-related science in Switzerland

The use-case approach to SPHN is based on experiences from the SPHN Driver projects. The description of a 'typical' work plan for a given use case is supposed to help future researchers to systematically address the procedural, infrastructural, ethical, legal and regulatory issues of personalized health research projects in Switzerland. Using the interactive SPHN webpage, the researcher can find the relevant partners, analytical platforms, SOPs, access to networks, regulatory processes and recommendations. An example of use case Category 1 is given in Figure 8.

The typical work plan also refers to recommendations and regulations of other related research bodies in Switzerland such as SNSF, SBP, swissethics, etc. Interestingly, it includes help and training tools such as for developing an ethics work plan and applications (Health Data Ethics Map, ethicalsystemsmap.hest.ethz.ch/map). We plan to design a use-case-specific SPHN data management plan template which facilitates the future application for research funding (e.g., SNSF proposals).

In summary, data structure and use cases' differentiation will help the SPHN community to discuss specific aspects of the very heterogeneous personalized health research in Switzerland in the upcoming years. It will also directly help the future researchers to practically profit from the experiences of the Driver projects and provide practical help in developing the work plan.

17. International Review and Gap Analysis from Intermediate Reports

Critical review of the progress was performed in 2019 based on the first milestone reports, an external international review by the International Advisory Board (IAB) and a gap analysis of the hurdles and systematic infrastructural problems based on feedback from the intermediate milestone reports.

The detailed report of the IAB is available on sphn.ch[18]. The main issues and recommendations are summarized below. In general, the IAB acknowledged that SPHN has made a good start and considered that none of the challenges are particularly surprising or insoluble. However, the challenges are real and require a focussed and sustained effort to solve them. The IAB is confident that the talented participants in the program will be able to overcome the barriers of bringing personalized medicine to the people of Switzerland. They made a few general recommendations, which are translated into action points and working groups in detail below:

- A meeting with the University Hospital leadership would be helpful to develop a common understanding of the utility of the initiative and agree on a common long-term vision and support provided to SPHN;
- A radical consolidation of procedures, processes and agreements at all levels – from consent, creation, management and access to data – is needed from the data controllers;
- Partner institutions should create a prioritized list of shared digital services for which there are clear economies of scale that each network node benefits from in terms of quality, functionality and cost;
- SPHN needs to consider how to support and engage the private sector e.g., at which stage, on which terms and how these can be developed to benefit all parties.

Several gaps in the SPHN infrastructure were identified during the review of the intermediated annual reports and while performing the mapping. These gaps are systematic hurdles which impede the majority of Driver projects and are summarized in Table 5.

18 www.sphn.ch/wp-content/uploads/2019/12/IAB_Review-Report_2019.pdf

Table 5: Identified Gaps.

SERVICES	Exists	Work in Progress	Gap	Quality and phase of implementation (PDCA cycle)
Funding, grants	×			4
Ethical guidance (documents)	×			3
Semantics & interoperability harmonization	×			
Events & comm. (incl. training)	×			3–4
Coordination, project management	×			3–4
Process innovation	×			3–4
Federated data query system		×		
Data interoperability between University Hospitals (organizational, legal aspects)			×	3
Data linkage centre			×	1–2
Patient & citizen involvement			×	2
ELSI helpdesk			×	1
Harmonization of *omics (standards, quality)			×	2
Inventory/catalogue of research infrastructure			×	2
PRODUCTS	**Exists**	**Work in Progress**	**Gap**	**Quality and phase of implementation (PDCA cycle)**
General consent (unimedsuisse, swissethics, SAMS)	×		implementation	3
Ethical Framework	×			3
Clinical semantics strategy & data sets	×		implementation	1
Data Transfer and Use Agreement template + Material Transfer Agreement template (SBP)	×		implementation	3
Authorship guidelines (a+)	×			3
IT security policy	×			3
E-consent, citizen-centred consent (dev. projects)		×		2
Guidance on the return of clinical actionable findings		×		3
Access & use policy (federated data query system)		×		
Data strategy 2.0			×	
Global IT strategy			×	
*Omics harmonization concept			×	
Unique patient ID			×	2
IP guidelines		× (initiated)		2
Guidelines regarding interactions with the corporate world (e.g., PPP)		× (initiated)		2
Map of research infrastructures		× (initiated)		2
Long-term and sustainable funding strategy of infrastructure			×	1

PDCA cycle (plan, do, check, act). Phase 1 (plan): defining the problems; Phase 2 (do): define measures to address the issues; Phase 3 (check): evaluates progress and gaps and adjusts; Phase 4 (act): defines mandates and working groups and redefines new standards.

Table 6: Identified Gaps and Potential Partners.

SERVICES		
Gaps	Infra. domains	Potential partners?
Data linkage centre	D, E	BAG, BFS, SNSF, FMH
Patient & citizen involvement	A, B	SBP, SCTO
ELSI helpdesk	B	SBP, SCTO, swissethics
Harmonization of *omics (standards, quality)	C, D, E	PHRT
Inventory/catalogue of research infrastructure	C, D, E	SBP, SCTO, PHRT, SNSF
Long-term and sustainable funding strategy of infrastructure	C, D, E	SBP, SCTO, PHRT, SNSF
PRODUCTS		
Gaps	Infra. domains	Potential partners?
Implementation of E-consent, citizen-centred consent	A, B	SBP, SCTO, swissethics, unimeduisse, SERI, FORS
*Omics harmonization concept	C, D, E	PHRT
Unique patient ID	A, B, E	BAG, FMH, SCTO, FORS, SERI
IP guidelines	B	SBP, SCTO, PHRT
PPP guidelines	B	SBP, SCTO, PHRT
Map of research infrastructure	C, D, E	SBP, SCTO, PHRT, SNSF

A: Patient or citizen oriented; B: Ethics, legal, data protection, patient information; C: Analytical platforms (e.g., genomics, metabolomics, proteomics, etc); D: Bioinformatics, medical informatics, big data analytic platforms; E: National registries, technology, and analytical networks.

SPHN has chosen three strategies. First: coordination with stakeholders; second: mandates and working groups (task forces); and third: recommendations (task lists) for partner organizations. During the gap analysis, there was increasing awareness that many of the identified issues and problems – including the lack of education and understanding in the field of data interoperability – were also relevant for other stakeholder groups (Table 6). Unsurprisingly, a number of uncoordinated boards and working groups addressing similar tasks already existed in the national research landscape. Following a number of bilateral agreements, these stakeholders agreed to coordinate the efforts. This agreement was supported by an official mandate of the SERI in November 2019 that SAMS should coordinate infrastructural efforts of SPHN, SNSF, SCTO, SBP, PHRT and SAKK. An overarching strategy paper ('white paper') was mandated to be elaborated by the SAMS to guide these efforts. Within the SPHN mandate, as a first step the stakeholders agreed that common working groups should be established – only one of the stakeholders takes the main responsibility to elaborate a position paper addressing a given task, which subsequently should be approved by the SPHN NSB and the governing boards of the partners. Such a position paper should then ideally be binding for all the involved stakeholders.

The second instrument involves mandates and working groups. In 2020, the initially established Scientific Expert Board was transformed into a more dynamic and focussed National Advisory Board (NAB). The NAB will guide and coordinate working groups which aim at fulfilling a given mandate. Mandates are created based on the gap analysis or novel needs identified by the NSB or the research community. With the third instrument of Recommendations (task list) for partner organizations, identified issues are addressed, which are not easily solvable with the SPHN consortium, but are in the core competence of the partner organization. Nevertheless, these issues are critical for the SPHN endeavour.

18. Issues to be Addressed in 2020–2021 by the Individual Stakeholders (Recommendations, Task List)

18.1. Mandated scientific SPHN working groups

The following mandates were defined and initiated in 2019:

1. Development of a concept for Patient and Citizen Involvement Think Tank (lead SCTO, patient organizations);
2. Development of IP guidelines (lead SBP);
3. Development of guidelines for collaboration with the corporate world (lead SPHN-ELSIag);
4. Development of the concept for a Swiss Federated Genomics Network (lead SPHN-NAB);
5. Development of the concept for a Swiss Federated Metabolomics/Proteomics Network (lead SPHN-NAB);
6. Development of a Data Lifecycle Management Strategy/Policy: Practices, standards and specifications for a Data Set Catalogue (lead SPHN-NAB). This working group should tackle all types of data: pictures, texts, streams, DNA… ;
7. Development of a Harmonized Swiss Cohort and Registry Strategy: Principles and Standards for IT-solutions & FAIR data (lead SPHN-NAB).

Detailed mandates, involved partners, timelines and working group members can be found on the SPHN homepage[19].

18.2. Hospitals (Recommendations)

The two major organizational obstacles of many SPHN projects were based on i) data format, organizational and legal inconsistencies between the involved centres, as well as ii) inconsistent views with respect to data sharing and data-access rights (data ownership). These two issues are critical for the entire SPHN initiative and have a critical urgency to be solved. The issues are detailed below:

1. Multi-dimensional use of health data. The discussion should evolve from the traditional paradigm research data vs. non-research data. Rather than creating silos, one should consider data as something that is useful for several groups (patients, research institutions, authorities, etc) and address issues from a broader perspective.
2. Heterogeneity of patient data. There is still significant heterogeneity within and between University Hospitals in terms of data availability, data formats, data protection issues, ethical and legal situation of patient-related data. This is crucial for data interoperability. In addition, there is an issue regarding the infrastructure that cannot be the same if used for research or diagnostics. Thus, this point requires stringent system controls to ensure correct analyses, even if used on the same data sets. Since it is legally difficult to centralize data (cantonal laws), the only solution to how quality assurance and interoperability of patient data can be ascertained is a common accreditation process. It is therefore recommended to elaborate a concept for implementation and controlling of the proposed SPHN standards (Clinical Data Semantic Interoperability group or IT interoperability group) and the SBP standards for biobanks. A labelling/accreditation process of databases and registries similar to SBP's should be considered. Finally, it may be of interest to more strictly separate the data acquisition process from the data usage process.
3. Prioritization of SPHN infrastructures within hospitals. It has been reported by researchers and Hospital IT responsible people, that SPHN-related issues are often not the priority of Hospital IT departments. Sometimes no clear mandates to develop SPHN requirements have been defined. In this context, the interfaces between Hospitals and BioMedIT should be re-evaluated. It is recommended to elaborate governance structures and prioritization of the proposed SPHN hospital IT infrastructures. In addition, it is important to mention that data management will become an integral part of medicine and research, independently of SPHN.
4. Financing of research infrastructures within the hospitals. There is uncertainty about how research infrastructures (biobanking, data warehouse, Hospital research IT) should be financed in the hospitals in the long term. This is imminent, since with increasing numbers of patients giving general consent for further use of data and biospecimens, the need for such storing infrastructures is rapidly increasing. Additional financial support is required to transfer data stored unprofessionally (e.g., Excel sheets) to reliable solutions. Funding of the research infrastructures could be tied to a certification/assessment process for data, registries and biospecimens.

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5. SPHN process support within hospitals. SPHN-related organizational structures in the hospitals have not been fully built up, or these organizational support structures are not known to the research groups. It is recommended to make these services available and visible. Ideally, these efforts are coordinated with the local University. This particularly involves clear funding and pricing agreements between the University and Hospital at the start of the project. The role of other structures such as SCTO or SBP as well as the local structures (CTU/CRC) or local biobanks in the support and communication to researchers and communities should be coordinated with the SPHN initiative.
6. Clinical versus research standards. In the clinical environment, many analytical processes require and follow international quality assurance standards (accreditation). In the research environment, other validation methods are used, mostly not consistent with the clinical standards. Processes (how analytical findings developed in a research environment can be translated to the clinical world) exist and need to be implemented in the new fields of personalized health. One of the upcoming documents (return of actionable findings) will cover some aspects of this field. The implementation of such recommendations needs to be organized by the University Hospitals, ideally in close collaboration with unimedsuisse. Funding to establish validation methods and processes should be made available.
7. Embedding of university partner hospitals. At many University Hospital sites, the infrastructures have been built up in the main campus, however, no connection to associated University Hospitals (children's hospitals, psychiatric hospitals, external surgical hospitals) has been considered.
8. Legal and ethical support structures between hospitals. SPHN-related multi-centre studies require complex data and biospecimen transfer agreements. The researchers spend large amounts of time and resources to overcome complex legal and ethical issues (weeks and months). Despite existing data transfer agreement templates, a major and time-consuming hurdle is the individual contracts between hospitals, which typically take months. Factors that impeded rapid solutions, were reported as:
   a. Strong local or cantonal legal particularities and requirements related to the involved University Hospitals;
   b. Limited personnel resources, low priority and lack of knowledge of the involved legal departments of the University Hospitals, fragmented approval strategy leading to information gaps;
   c. Lack of project management skills and legal knowledge of the PI of these multi-centre studies;
   d. Lack of a national legal support service, and lack of successful examples how given use cases could be handled (legal framework agreements of specific use cases, see chapter 12);
   e. Lack of examples regarding how the requirements of Open Data can be applied to multi-centre studies;
   f. Authorship Guidelines should be revised and reflect on the definition of a scientific contribution in the 21st century.

It has been proposed by several researchers that a nationally steered consortium of hospital legal specialists is set up, which could help large, multi-centre, big-data studies to facilitate the data transfer and biospecimen agreements (nationally coordinated legal help desk). Such an experienced board could be trained in the specific legal topics (as well as on the objectives of the initiative) and could even elaborate examples of legal framework solutions for given use cases, which have led to successful data transfer in the past. SPHN follows this recommendation. A national legal help desk may be useful, but will not resolve the problem of different attitudes of the cantonal ethic committees. A harmonization of the different cantonal applications must be obtained through a transparent monitoring of their activities.

9. Organizational and legal templates for a given PH-research use case. In order to do so, standardized 'use cases' need to be exemplified, which can then be followed for future projects. SPHN should try to define such use cases. An attempt of such use cases based on the current SPHN and PHRT projects can be found Section 15.3.
10. Data sharing, data-access rights and roles of partners within a multi-centre project are known to be difficult to solve. SPHN recommends a realistic approach to this complex issue, these issues strongly depend on the nature of the data, the involved stakeholders and their degree of pre-processing and quality control of the data. Some SPHN and PHRT projects are based on poorly structured hospital data (data mining approach), and some projects are based on prospectively sampled structured data (cohort- or registry-type data). The SPHN system should be built up such that it can support researchers dealing with both types of data, however, processes and data-sharing principles might realistically differ between these different types of data. A one-fits-all approach may not address all the needs of the research community. Data-sharing principles may depend on the type of data. A focussed discussion may be helpful to improve data sharing and defining of research partners.
11. Sustainability of hospital research infrastructures. Many of the involved hospital research structures are now being built up during the SPHN periods

2017–2020 and 2021–2024. However, it is recommended that hospitals elaborate funding and infrastructure concepts (data warehouses, biobanks, support processes) to make these efforts sustainable after the end of SPHN in 2024. In the long term, returning results to individuals should also be possible and efforts to make this possible are needed. Further, a coherent research policy where the boundaries of clinical research are better defined should be developed by swissuniversities. This will help to structure the national research and clinical research landscape.

18.3. Universities, ETH Domain (Recommendations)

Many researchers have reported issues that occurred at the interface between local universities and the related hospitals. SPHN identified the following issues:

1. Clear responsibilities, cost structures, access policies and funding of PH-analytical platforms need to be defined and ideally harmonized within Switzerland;
2. Clear responsibilities, cost structures, access policies and funding of PH research, biobanks, data warehouse at the interface of University Hospitals and local universities need to be defined;
3. On-site support structures and services for scientists in personalized health and precision medicine research need to be prioritized to provide the necessary support.
4. This includes facilities for project management and budget control of large-scale research projects including realistic cost estimates of platform use;
5. Many of the involved university research structures are being built up during the SPHN period 2017–2020 and 2021–2024. However, it is recommended that hospitals in collaboration with universities elaborate funding and infrastructure concepts (analytical platforms support processes) to make these efforts sustainable after the end of SPHN in 2024;
6. Despite the organization of events and information on the SPHN website, the SPHN's funding schemes are still not well understood by researchers: SPHN is different from other funding schemes as it is a research infrastructure program. Further efforts are needed in the next funding period.

18.4. Government, Politics (Recommendations)

SERI has asked SPHN to develop a list of political and legal issues that hinder biomedical research. In collaboration with all the partners, SPHN has identified critical issues which have a legal or political dimension. These issues are highlighted in Table 7.

There is an urgent need that these issues are addressed in a timely manner and that political groups address the issues of personalized health for the benefit of the healthcare system of the country. Issue 1 and Issue 2 are mandatory prerequisites for a successful personalized health system in Switzerland and significantly facilitate infrastructural processes, data quality and patient data protection issues.

Table 7: Political and Legal Issues Hindering Biomedical Research.

Issue	Description
Patient ID for research (law change)	The Human Research Act allows the further use of biological material and health-related data for future research projects, provided that the data is coded. One possible method of encryption is to use an algorithm that generates a unique, individual "research number" from the patient's AHV number, which cannot be traced back to the AHV number. The AHV number is then deleted from the "generation system".
E-consent/E-signature for research (law change)	A handwritten signature (wet ink) is required when giving consent which prevents PH research. However, the Postal Ordinance allows for electronic signature on a device. The HRO should thus be amended accordingly.
Disclosure of medical information (political and legal issue)	Individuals are obliged by law to disclose medical information gathered during a project. As this information can be used against them and prevent them from contracting insurance (e.g., life insurance, sickness insurance for self-employed people, 2nd pillar, etc.), this can be a disincentive to taking part in research projects. There should be a reflection and political discussion at the national level about whether citizens should be encouraged to participate in research to improve health research and whether the law should be changed to protect participants from discrimination.
Secondary use (political and legal issue)	Some European countries such as Finland have changed their law such that the further use of health data can be used for research and quality improvement of the health system by default, without active consent of the patients. This legal framework allows the country to foster the development in personalized healthcare significantly. In Switzerland the values of data protection and individual consent are culturally important. Thus, the SPHN initiative has so far based its efforts on the principle of consented data. However, it needs to be politically discussed whether the Finnish legal framework might be an option for Switzerland in the future. It may also allow better quality research in the Swiss health system.
Need for a large-scale national cohort (political)	As genome analysis becomes mainstream for research and clinics, Switzerland has many things to offer in terms of scientific strength, quality of the health system including universal coverage and detailed patient phenotyping. A Swiss large-scale cohort spanning healthcare and research (e.g., in a particular disease field or focussed on healthy citizens in the form of a health reference cohort) would significantly contribute to strengthening Switzerland's status as a research centre as well as driving transformative change and widespread clinical implementation. Building up a national cohort is not in the primary mandate of SPHN, neither of PHRT. However, during the first phase it became apparent that both initiatives feel responsible for bringing this significant need to the political agenda. In addition, SPHN and PHRT offer support in conceptualizing and initiating the first steps in direction of a large-scale national cohort.
Framework agreement with the EU (political)	In case Switzerland does not sign the Framework agreement with the European Union, collaborative projects with EU partners might become more difficult. In addition, Switzerland might no longer be allowed to participate in consortia such as ICPerMed.
ERA-NET in Personalized Medicine (ERA-PerMed) (political)	Although Switzerland is part of the International Consortium for Personalized Medicine (ICPerMed), it is not taking part in the corresponding ERA-NET funding program ERA-PerMed: SPHN is not allowed to participate in the ERA-NET as the funds must remain in Switzerland; The SNSF was not interested in taking part in this ERA-NET. Given that in Horizon Europe, a partnership between ICPerMed and ERA- PerMed is foreseen to create a co-fund program, it is essential that Switzerland can apply for funding from ERA-PerMed. It should thus be clarified with SNSF, the Academies or other funders who will take this role.

19. Benchmarking of SPHN Based on the EU-Commission and the ICPerMed Vision and Action Strategy

The progress of personalized health research in Europe is very heterogeneous. Typically, countries with a centralized healthcare system and a legal framework allowing facilitated access to health data (such as e.g., Finland, Estonia, the Netherlands and parts of the UK) are dominating the personalized health landscape in Europe. Nevertheless, the fundamental issues of data sharing, data protection, consent management, semantics, interoperability, return of actionable findings etc. are ubiquitous in all countries. The local individual solutions are related to the cultural, legal and political context of these countries. Nevertheless, SPHN achievements and goals should be benchmarked with the visions and strategic goals defined by the European ICPerMed Consortium.

Vision 1: Informed, Empowered, Engaged and Responsible Citizens

The SPHN funding period 2017–2020 has focussed on technical and legal feasibility and infrastructure building and consensus finding. Although members of both the NSB and the ELSIag were representative of patient organizations, in the upcoming funding period, patient involvement needs to be a major focus of the SPHN initiative. Nevertheless, dialogue programs with patients and citizens need to be established. Current efforts have linked existing information portals for citizens to the new homepage of SPHN and contact with Science & Cité (www.science-et-cite.ch) have been initiated.

Vision 2: Informed, Empowered, Engaged and Responsible Health Providers

SPHN is embedded in SAMS and representatives of unimedsuisse are in the National Steering Board of SPHN. In the funding period 2021–2024, the interaction with the industry-based health providers and health insurers is a planned focus area. Particularly in the area of technical standard, SPHN should profit from knowledge available in the pharmaceutical and big-health-data industry.

Vision 3: Health Systems Enabling Personally Tailored and Valuable Health Promotion, Prevention, Diagnosis and Treatment for the Benefit of Citizens and Patients

Several SPHN Driver projects (e.g., Frailty) have provided data, processes and infrastructures to bring better tailored diagnostics and treatment strategies to patients in specific disease areas. It will be a challenge of the next funding period to implement and link these infrastructures to the clinical decision processes.

Vision 4: Availability of Health-Related Information and Data for Valuable Treatment, Care, Prevention and Research

SPHN has, in its initial phase, focussed on University Hospitals and on health-related information and data primarily for research. Nevertheless, individual Driver projects (e.g., SPO) have already used these data for facilitated treatment decisions and care. The readiness of the system for the healthcare sector depends on the degree of implementation of the newly built infrastructures, where oncology seems most advanced in the field. SPHN should not only provide input for research in diseases but ultimately for salutogenesis and prevention. One Project (SACR) explores the possibility of including citizen data into the SPHN network. In the funding period 2021–2024, a focus will be placed on incorporating citizen-centred data.

Vision 5: Economic Value by Establishing the Next Generation of Medicine

SPHN has not addressed the economic considerations of personalized medicine in Switzerland. This was not in the initial mandate. Nevertheless, during the funding phase 2017–2020, it became evident that a certain economy of scale needs to be considered during the process of infrastructure building and considerations related to value creation in precision value (see chapter 24) need to be addressed in the future. The issue of sustainability of the initiated infrastructures will be critically dependent on their costs and the created benefit for the healthcare system as well as the related economic value.

20. The Need for Implementation Strategies

During the funding period 2017–2021, one of the biggest challenges for SPHN infrastructure building is the stringent implementation of the defined and agreed standards, semantics and infrastructures. Implementation and sustainability will be the major themes in the funding period 2021–2024. Several principles and instruments to foster nationwide reliable implementation have been discussed.

20.1. Alignment of stakeholders' goals and stakeholder commitment

Several efforts have been made to align the interests of SPHN, PHRT, SBP, SCTO, SNSF, swissuniversities, unimedsuisse, swissethics and patient organizations. SPHN and PHRT, SBP and SCTO have aligned their goals for the next funding period. Agreement on common standards have been made and references and links between homepages have been established to increase stringency of recommendations and procedures.

20.2. Economy of scale

SPHN cannot fund all the infrastructures, particularly not in a sustainable manner after 2024. SPHN can support infrastructures, where most stakeholders can profit and where interoperability is facilitated, e.g., a data query systems across all University Hospitals will be used by all research groups, facilitated data transfer and access points to analytical platforms, a safe and legally appropriate IT environment where big data sets can be stored and analysed using bioinformatics, will be needed by many projects. Such infrastructures can be provided by SPHN and BioMedIT; these can be maintained most cost-effectively on the national scale. On the other hand, the maintenance and quality control of specific databases (e.g., cohorts, registries), disease-specific platforms, or research projects embedded in such IT infrastructures need to be funded and processed by local services or consortia.

20.3. Measuring implementation and progress

The annual activity and financial reports of the projects (infrastructure development and driver projects) and the collaboration agreements are due by 31 March every year.

Each SPHN Board reviewed specific aspects of the projects based on their expertise:
- Assessment by the MO regarding the use of SPHN funds and matching contributions;
- Recommendations from the ELSI advisory group (ELSIag) regarding progress made with respect to the implementation of the guidance outlined in the Ethical Framework for Responsible Data Processing in SPHN including data sharing;
- Assessment made by the Data Coordination Center (DCC) regarding the technical milestones and collaboration with respect to standards and semantics.

The main points of each review were reported in a table and a traffic light rating system was used for indicating whether the conditions for releasing the next payment were met (green=met, orange=partially met and red=unmet).

After collecting the reviews of the SPHN Bodies, the NSB Ausschuss examined the comments and assigned an overall rating for each project. This rating determines the conditions for the next payment as outlined in Table 8.

Table 8: Funding Continuation Principle.

Overall rating	Description
Green	– Full payment of the next installment (all financial questions must be clarified before payment);
Orange	– 50% of the next installment (all financial questions must be clarified before payment); – The remaining 50% are paid, provided the issues are addressed within the next 6 months from the date of notification; – If not addressed, the project turns red.
Red	– No payment; – Applicants have to provide an explanation in writing and a timescale to address the issues; – The applicants are invited for a meeting with the Ausschuss.

Based on the overall progress made, the NSB Ausschuss submits a recommendation regarding the payment of the next installment to the NSB. The final decision on releasing the next payment is taken by the NSB and communicated by the MO.

20.4. Quality assessment of the SPHN program (PDCA cycle)

Following the gap analysis, the NAB and the SPHN implementation teams will have to monitor the quality of the implementation using established quality measures following e.g., the PDCA cycle (plan, do, check, act). This involves Phase 1 (plan): defining the problems, Phase 2 (do): defining measures to address the issues, Phase 3 (check): evaluating progress and gaps and adjust, and Phase 4 (act): defining mandates and working groups and redefining new standards.

20.5. Adherence to agreed standards and data-sharing principles – SPHN, SBP quality labels

Research quality standards, data and biospecimen standards, safety standards and ELSI standards need to be maintained in order to improve quality of research in precision medicine. They are prerequisites for the interoperability of health data. SPHN initiates a process to define such standards and recommends their implementation. A discussion about whether institutions fulfilling these national standards should receive a SPHN quality label is needed. SBP has started to implement labels for biobanking. Ideally these SBP labels should also be adopted for SPHN and have validity in the SPHN context. These issues need to be discussed and decided in the SPHN NSB in the near future.

In this respect, research funders (e.g., SNSF) will have an important role – their strict recommendation to use such high-quality standards and SPHN platforms will be instrumental for success.

20.6. Building national data streams and technology or disease-specific multi-omics platforms

European Countries advanced in personalized health (such as the Nordic and Baltic countries) have started to create thematic national platforms enabling both research as well as molecular boards supporting patient care (e.g., FICAN, National Cancer Center Finland). Similarly, in Switzerland, SPHN Driver projects with a common thematic focus have started to collaborate and formulated the need for national coordination and platform building. Such platforms have the following advantage:

- They foster multi-omics approaches;
- Optimization of resources in the specific field;
- Account for specific needs of a given topic;
- Coordination of health-data sharing and define disease-specific governance rules in a specific field;
- Definition of measures (infrastructure, business plans) to maintain sustainability of such platforms.

20.7. Sustainability after 2024

The most critical issue of the SPHN initiative relates to the sustainability of the newly built infrastructures. The funding period 2021–2024 must prioritize such considerations. Hereby the following principles must be considered:

- Clear alignment of the involved stakeholders and definition of responsibilities (SERI, hospitals, universities etc.);
- Economy of scale;
- Clear vision on socket infrastructural costs in relation to costs related to the research projects running on such infrastructures;
- Business plans with clear pricing schemes for infrastructure and analytical platform use;
- Utility of such platforms for clinical use, health economics consideration;
- Value creation in precision medicine and personalized health (see below).

21. Outlook into Funding Period 2021–2024

Based on the progress and identified gaps from the funding period 2017–2020, the following general directions have been identified and agreed on (see also Table 9 for examples of aspired goals and deliverables for the next SPHN funding period):

To consolidate the existing infrastructure and prepare the network to include additional hospitals and, ultimately, general practitioners.

During the second phase, the infrastructure developed at the five University Hospitals should be consolidated and the network should be prepared to progressively include additional hospitals, and ultimately, general practitioners (private practices).

To this end, different mechanisms of exchange should be explored for feasibility and scalability such as:
- Mapping and visualizing the existing patient-oriented research infrastructures (in close collaboration with partners such as SBP, SCTO, PHRT, etc);
- Elaborating strategies and principles to facilitate sharing structured and unstructured clinical and research data;
- Structuring data using common semantic standards (5 University Hospitals);
- Indexing of non-harmonized documents (e.g., CREATE Prima project);
- Reusing clinical data exchange mechanisms (e.g., EPD, FOPH, eHealth Suisse);
- Defining access points, interfaces and data transfer standards to existing analytical research platforms (e.g., genomics platforms).

To pursue efforts with respect to expanding the scope of clinical variables and accessible data sources.

By 2020 numerous clinical variables and data sources will have been integrated in the SPHN framework. This endeavour should be continued in the next period to include:
- Complete clinical data sets (e.g., imaging, *omics [in collaboration with PHRT], lab values, patient history, free texts), including multi-omics sets (where available);
- Information from cohorts/healthy citizen data (in collaboration with SNSF), and biobanks (in collaboration with SBP) allowing not only research in pathogenesis but also prevention of diseases (salutogenesis);
- Longitudinal and transgenerational data allowing elucidation of disease trajectories;
- Statistical data (e.g., BFS);
- Patient-reported data, telemonitoring data;
- In addition, international collaborations to ensure interoperability at the international level should be further developed (e.g., UK Biobank, NaKo and Medizininformatikinitiative Germany).

To develop procedures to increase usage of citizen-controlled data and to make sure that it is interoperable with hospital data. Collaboration with cohorts is envisaged, however, it should be limited to infrastructures and processes to facilitate interoperability, which can e.g., be achieved by coordinated data formats and semantics.

The amount of non-clinical data generated by each individual is increasing rapidly. As SPHN embraces a holistic view of the patient/citizen, mechanisms to make these data interoperable in the SPHN system are needed.

This involves the development of citizen-centred general consent strategies, which should be coordinated with hospital-based general consent strategies (further use of clinical data).

Further, SPHN needs to employ data management systems which ensure autonomy/privacy for citizens and allow for efficient data use (SPHN should collaborate with organizations working on the implementation of the Electronic Patient Dossier (EPD) and patient data cooperatives).

The FOPH is supporting the “Schweizer Gesundheitsstudie” (biomonitoring cohort) which is currently in its pilot phase; this study is planned to be scaled up and continued during the period 2021–2024. SPHN should thus collaborate with this project on establishing common data infrastructure to ensure interoperability of information. Further, SPHN should contribute to the interoperability of the “national cohort” as part of the FOPH Non-Communicable Disease Strategy.

To strengthen the SPHN ELSIag in its function as a sounding board for SPHN, and with respect to its role in the implementation of guidelines in the research settings, and in fostering engagement with patients and citizens.

As the SPHN project matures from research infrastructure projects to clinical applications, SPHN needs to strengthen its efforts on ELSI aspects. It is essential to put the patient/citizen at the centre and to inform them about their rights:

- Processes, support structures and teaching tools, which facilitate the administrative burden of patient-oriented research for the individual researcher, need to be established.
- Principles to regulate return of actionable research findings into the clinical context need to be elaborated.
- Further, infrastructures and processes to facilitate patient and citizen dialogue should also be developed.

To develop a strategy for the interaction with international consortia and the corporate world (e.g., industry studies).

During the first phase of SPHN, several commercial entities and international consortia approached SPHN and showed great interest in collaborating with the initiative. To date, informal discussions have been held, however, no partnership has been established.

Conditions and mechanisms for fair collaborations between SPHN partners, commercial entities and international consortia should be defined. General guidelines on how to interact and regulate projects with the corporate world in the SPHN context should be elaborated.

To establish the concept, governance and technical platform for a long-term, independent national centre for health-data coordination and infrastructure for research from 2024 onwards.

SPHN establishes infrastructures, competences and processes for personalized research in Switzerland, which need to be sustainable after the end of the initiative.

The SPHN Data Coordination Center should evolve to become an independently functional 'national competence centre' by the end of 2024. This platform will provide a technical solution to allow the hosting of encoded hospital, citizen-centred and cohort data in an interoperable, legal, safe and semantically harmonized form. The envisaged profile of the competence is the following:

- To define a concept, governance structure and business plan of such an independent centre accounting for economy of scale (basic socket infrastructure costs, pricing for project-based data infrastructure use etc.);
- To provide central technical IT infrastructure (e.g., for cohorts and research data) in close collaboration with DCC and ETH Domain;
- Define an overall IT-Strategy for the exchange and storage of health research data;
- To define the data-access rights and data-sharing principles of such an independent national centre for health-data coordination;
- To define a guideline on lifecycle of health research data;
- To maintain a national data catalogue and coordinate a network of federated data resources;
- To develop and implement (inter-)national policies and quality and data standards.

Throughout 2017–2020, it became obvious that we needed to prioritize the issues of mandatory implementation, sustainability, public trust, data availability, interaction with the clinical world and health economy and interaction with the corporate world.

Table 9: Examples of Aspired Goals and Deliverables for the Next Funding Period 2021–2024.

Addressee / Field/topic	Aspired goals/deliverables
Swiss hospitals	
Data findability	– Clinical data of hospitals is findable through the SPHN data catalogue and the federated query system; – Available patient-centred data sets are indexed in the Swiss meta-data catalogue.
Data accessibility	– Clinical data can be requested through the SPHN data request portal; – Governance processes are transparent and streamlined; – Pre-approved templates for legal agreements concerning collaboration, data transfer and use, etc. contribute to shorter waiting times in the signature process; – Data delivery of research data takes place within the agreed time.
Data interoperability and quality	– Research data is delivered according to the SPHN semantic framework standards and requirements, also outside of SPHN; – Structuring, standardization and coding of data happens at the timepoint of data capture (at the source); later mapping becomes the exception; – Frequently used and internationally recognized standards (e.g., coding systems and controlled vocabularies) have largely replaced local and national standards; – Clinical data in high-quality (encompassing completeness, consistency, validity and accuracy) are available for data-driven research.
Data reusability	– Data access processes for reuse are transparent and harmonized; – Common data-sharing principles in relation to the type of data are established and being followed.
Sustainability of infrastructures	– A long-term strategy for further developing and maintaining research infrastructures in hospitals (biobanking, data warehouse, hospital research IT) is implemented.
Research community / BioMedIT	
FAIR biomedical data for research	– A FAIR data management strategy is implemented; – A harmonized Swiss cohort and registry strategy is implemented; – A federated *omics network enabling sharing and processing of genomic, transcriptomic, proteomic, and metabolomic data for research is established; – A Swiss meta-data catalogue to find and access patient-centred research data sets is established.
Quality of data	– High-quality (structured, curated and contextualized) data sets are available for research in Switzerland.
SPHN network	
	– A business plan including a long-term funding scheme for an independent "National Center for Health Data Coordination and Infrastructure for Research" is established; – Guidelines for public/private partnerships for ethical health-data access and processing facilitate interaction and collaboration with the private sector in the context of PH and set standards for engagement; – An open dialogue, the involvement of patient-perspectives, transparency and knowledge-building measures support trust and a positive attitude towards data sharing for research purposes and clinical research in general; – Guidelines to help researchers assigning intellectual property rights in the frame of collaborative PH projects.
Desired parallel developments beyond the scope of SPHN	
	– A Swiss large-scale cohort spanning healthcare and research is funded, contributing to strengthen Switzerland's status as a research centre as well as driving transformative change and widespread clinical implementation; – The general consent is tied to the patient, rather than to a hospital; – A unique identifier is available to be used in research, and a Swiss linkage/trust-centre is established.
Overall goal	
	– Healthcare and research go hand in hand in the digital learning healthcare system of tomorrow.

22. A Long-Term, Independent National Center for Health Data Coordination and Infrastructure for Research (2024)

To achieve such an infrastructure is a highly demanding task and its feasibility will very much depend on the willingness of the stakeholders to cooperate on this endeavour. Nevertheless, if it can be achieved, the shared benefit is significant and may help Switzerland to become one of the leaders in the field. Similarly, the healthcare system will also certainly profit from such a structure. This endeavour will not only foster novel diagnostics and therapies in precision medicine and personalized health, it will also improve quality of care, due to a better database that enables improved hospital organization and quality control. According to their recent report, the latter has been an important goal of FOPH (6). However, it also requires a change in cultural values towards a 'learning healthcare system' (see below). In order to foster such a cultural change, it is utterly important to carefully define an institution-independent governance of such a centre with well-defined access rights based on a legally and ethically appropriate framework. This is mandatory for public trust, if this cannot be achieved, citizens, particularly patients and hospitals, are not likely to share their data.

The question of centralized versus decentralized data storage needs to be addressed at an early stage. Advantages and disadvantages of either approach may depend on the use case (see above). Data quality can typically be better achieved in a centrally organized data set.

In order to establish sustainability of such a centre, a clear business plan with a long-term funding scheme needs to be established. The principles of economy of scale are important in this context. A separation of socket infrastructure maintenance costs (e.g., providing a secure IT environment) and research-project-related costs (data mining, cohort hosting, quality control, analytics etc.) need to be clearly defined, separated and priced. Experiences of previous research infrastructures (e.g., SCTO) suggest it is likely that socket infrastructure maintenance costs cannot be reduced to zero even in the long term and cannot be financed by the hospitals.

23. Critical Reflection of the Progress

SPHN has used a mixed top-down and bottom-up approach to address the issue of big-data-related research in precision medicine and personalized health. Probably the biggest achievement of this period is the increasing awareness of the systemic gaps and problems related to the field. Particularly, the gap analysis from SPHN Driver projects of the funding period 2017–2020 revealed significant obstacles, most of them related to the federated healthcare system and the strong local awareness and particularities of data protection issues as well as ethical and legal priorities. Although these features are culturally and politically deeply anchored in our society, they could become critical for the success of the endeavour. Similarly, the role of the cantonal and national regulators becomes critical. In order to achieve interoperability, data protection issues and data-sharing policies as well as ethical and legal priorities need to be coordinated on a national level.

The willingness of the stakeholders to agree and implement common strategies, standards and guidelines is a prerequisite. The political discussion needs to be initiated whether or not this should be enforced. Similarly, the political discussion related to the shared benefit of a data-driven health research and healthcare for Swiss society needs to be initiated.

24. Impact on the Healthcare System: Value Creation in Precision Medicine

Personalized health and precision medicine are dependent on large data sets from interoperable, harmonized, high-quality clinical data and related multi-omics analytics. However, it requires a digital ecosystem that sustains a suitable data value chain. The global value levers (7) are stakeholder collaboration and regulation (licencing and payment). SPHN can help to address the first important issue. Innovative collaboration among scientists, clinicians and partners (e.g., payers), patient engagement across the life cycle, interaction with the corporate world, early engagement with the clinical hospital and laboratory world (return of actionable findings) and finally with the payers are important to foster value-based decisions related to new diagnostics and treatments. However, the regulatory aspects and public trust are similarly important and outside the SPHN mandate. For the health economy it becomes more-and-more evident that a data-driven approach may help to transform the current healthcare system into a more data-driven learning healthcare system.

25. Conclusion

The funding period 2017–2020 was instrumental for stakeholder alignment, the building of technical infrastructures, process innovation, harmonizing of standards and interoperability. But most importantly, the Driver projects have elucidated the difficulties and gaps in the system. This is mainly related to the federated healthcare system with its local legal, ethical, and regulatory frameworks. Interoperability, and thus big-data health science is critically dependent on nationwide harmonization of these regulatory fram eworks. All stakeholders – including patient organizations, regulators and politicians – need to closely collaborate and develop a common understanding of these issues. Such a mind shift is a prerequisite for the development of health and biomedical sciences as well as healthcare and prevention at the next level in Switzerland. In order to build up a sustainable health-data-research infrastructure, stringent and coordinated implementation strategies and public dialogue are important key efforts for the next funding period.

26. References

1. Meier-Abt PJ, Lawrence AK, Selter L, Vayena E, Schwede T (2018). The Swiss Approach to Precision Medicine. Swiss Medical Weekly, Published 02 January 2018 in Op-eds.
2. DEG Report: Roadmap to achieve nationwide interoperability of health-related data (2018). SPHN Data Expert Group.
3. Ethical Framework for Responsible Data Processing Within SPHN (2018). ELSI Advisory Group of SPHN.
4. Report on the Implementation of the Swiss Personalized Health Network (SPHN) Initiative (2015). SERI commissioned Report by Working Group "Meier-Abt-ppel-Frey-Günther, Mooser-Probst-Hensch-Röthlisberger-Vonder Mühll".
5. Fried-Michael Dahlweid, Matthias Kämpf and Alexander Leichtle (2018). Interoperability of laboratory data in Switzerland – a spotlight on Bern. Journal of Laboratory Medicine J Lab Med 42(6): 251–258.
6. Federal Office of Public Health (2019). Health2030 – the Federal Council's health policy strategy for the period 2020–2030.
7. Nursimula A (2019). Value Creation in Precision Medicine: Acknowledging the Need to Devise New Ways to Measure The Value of Healthcare (a scoping review and annotated bibliography). Lausanne: EPFL International Risk Governance Center & Health 2030.

Appendix I: Finances

In order to build up such research infrastructures, the Swiss federal government (State Secretariat for Education, Research and Innovation [SERI] and the Federal Office of Public Health [FOPH]) has mandated The Swiss Academy of Medical Sciences (SAMS) and the SIB Swiss Institute of Bioinformatics to build the federal Swiss Personalized Health Network (SPHN) initiative. These two bodies are responsible for the implementation of the mandate, which has been allocated a total of CHF 68 M for the period 2017–2020. A follow up funding period is planned for the period 2021–2024. All the amounts mentioned in this chapter relates to the 2017–2020 funding period.

As described in Section Capacity Building, the SPHN initiative supports the development and implementation of coordinated infrastructures based on a three-pillar funding strategy:

1. **Top-down funding**
   - 1.1. Infrastructure implementation projects: Throughout collaboration agreements, 15 mio CHF have been allocated to the 5 university hospitals;
   - 1.2. SPHN Data Coordination Center: 2.82 mio CHF have been allocated to the DCC;
   - 1.3. Ethical, Legal and Societal Implication Advisory Group (ELSIag): 260k CHF have been allocated to fund ELSI support staff.

2. **Bottom-up funding**

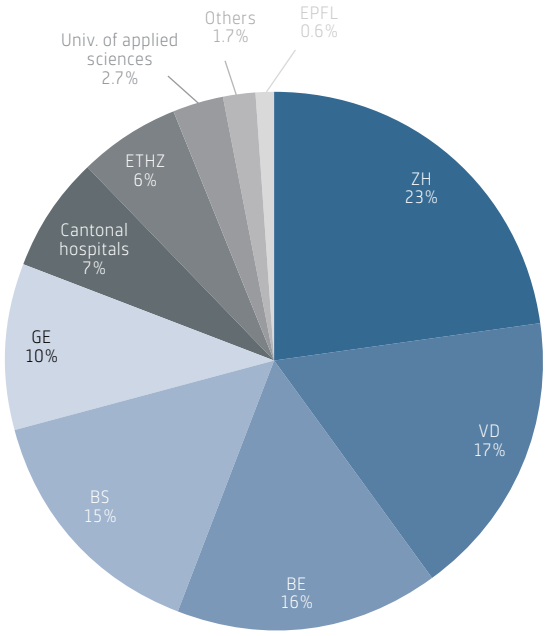
   In 2017 and 2018, two SPHN Calls for Proposals were organized in close coordination with the Strategic Focus Area 'Personalized Health and Related Technologies' (PHRT) of the ETH Domain'. Selected from a total of 76 proposals requesting CHF 90.4 M, SPHN funded 24 projects (incl. 6 co-funded by PHRT). CHF 25.3 M have been allocated to these 24 projects.

   Figure 9 shows the detail of the allocated funds by institutions (based on the addition on each individual project initial budget).

3. **IT infrastructure networks**

   18 mio CHF have been allocated to BioMedIT.

Figure 9: Infrastructure development projects and Driver projects – allocation of funds per location.



	Allocated amounts (in kchf)	Projects involved (n=24)
Universities and University Hospitals		
ZH	5738	17
VD	4323	17
BE	4066	15
BS	3908	16
GE	2680	16
Cantonal hospitals	1730	7
ETHZ	1601	9
Univ. of applied sciences	683	3
Others	430	11
EPFL	150	2
Total	25 309	24

Institutions involved in SPHN projects
ZH: USZ, UZH, KISPI UZH, Triemli · **VD:** CHUV, UNIL, HOJG · **BE:** Inselspital, UNIBE, UNIBE/Inselspital · **BS:** USB, UNIBAS, Swiss TPH, UKBB, FPS · **GE:** HUG, UNIGE · **Cantonal hospitals:** EOC, HVS, IOR, KGB, KISPISG, KSA, KSBL, KSL, KSSG, KSW · **ETHZ:** ETHZ, PSI · **Univ. of applied sciences:** BFH, HES-SO · **Others:** SIB, MIDATA Cooperative, SBP, SCTO, SICHH, Swiss Paraplegic Research, SwissPedNet · **EPFL:** EPFL

Appendix II: Data Types

Depending on the initial clinical or research purpose of the health-data collection, and dependent on the degree of structuring and quality motivated pre-processing, data sets can be grouped into different categories:

1. Clinical data extracted from clinic information systems into data lake;
2. Basic routine data (core data set);
3. Specific routine data (extended data set, e.g., disease specific);
4. Specific routine data (imaging data, lab data);
5. Clinical data registries, inclusive HSM (Hochspezialisierte Medizin Register);
6. Cohorts;
7. Clinical study data (clinical research project, clinical trial and clinical observational study data);
8. Patient self-reported and wearable device data;
9. Molecular or -omics data (generated in the hospitals, clinical grade);
10. Molecular or -omics data (generated in the research facility, research grade);
11. Citizen/Consumer health data, lifestyle data, social media data, wearable devices;
12. Reference data sets of all kind (environmental data, potential exposure to noxious agents, geographical data, statistical data…).

Different health-related research data can further be characterized based on the following criteria:

ii. Type of data;
xi. Original purpose;
xii. Degree of processing;
xiii. Degree of structuring;
xiv. Quality control;
xv. Data protection status;
xvi. Return of actionable findings;
xvii. Data governance and ethics requirements;
xviii. Related research stakeholders;
xix. Utility for PH Research, utility for clinical research;
xx. IP scenario recommendation.

For each data type examples of SPHN and PHRT projects are presented (where applicable). The further use of these data will depend on the above-mentioned criteria and needs to be defined for each category (Table 10).

Table 10: Data Types.

Type of data	Original purpose	Degree of structuring	Degree of processing	Quality of data	Degree of linkage to patient identity
Definition for headlines	Purpose for which the date is/was initially captured	The degree to which the data is structured in the context of the original use (unstructured, mainly structured, structured, highly structured)	The degree of processing required to make data interoperable for research (low, medium, high)	Quality of data from a research perspective, encompasing completness, consistency, validity and accuracy (low, medium, high)	The degree of linkage to patient identity in the original data collection (anonymous, coded/de-identified, identifying)
Hospital clinical data (routine data)					
Clincial data extracted from clinic information systems into data lake	Clinical use	Heterogeniously structured, unstructured	Very hight	Low to medium, heterogeneous (medium for clinical purpose, low for research purpose)	Identifying
Basic routine data (Core dataset)	Clinical use	Mainly structured	High	Medium heterogeneous	Identifying, but coded after transfer in datawarehouse
Specific routine data (Extended dataset, e. g. disease specific)	Clinical use	Structured or unstructured	High	Low to medium, heterogeneous	Identifying, but coded after transfer in datawarehouse
Specific routine data (imagine data, lab data)	Clinical use	Mainly structured	Medium	Medium	Identifying, but coded after transfer in datawarehouse
Clinical data registries, inclusive HSM (Hochspezialisierte Medizin Register)	Clinical use mainly in specific disease areas, standardized clinical parameters, quality and monitoring of patient care	Mainly structured	Low	Medium	Identifying, but coded after transfer in datawarehouse
Clinical research data					
Cohorts	Primarily assessed for research purposes	Highly structured	Low	High	Coded/de-identified
Clinical study data (Clinical research project, clinical trial and clinical observational study data)	Primarily assessed for research purposes	Highly structured	Low to medium	High	Coded/de-identified or anonymous
Patient self reported and wearable device data	Primarily assessed for research or quality purposes	Structured or unstructured	High	Medium	Identifying
Molecular data					
Molecular or -omics data (generated in the hopsitals, clinical grade)	Clinical use	Structured	Low to medium	High	Identifying or coded/de-identified
Molecular or -omics data (generated in the research facility, research grade)	Research use	Structured	Low to medium	Medium	Coded/de-identified
Healthy citizen data					
Citizien/Consumer health data, Life style data, Social media data, wearable devices	Divers	Structured or unstructured	High	Divers	Identifying
Reference data					
Reference data sets of all kind (environmental data, potential exposure to noxious agents, geographical data, statistical data…)	Divers	Structured	Low	High	Anonymous

	Return of actionable findings	Data governance, ethics requirements	Related research stakeholders and potential collaborative partners	IP scenario recommendation (SPHN DTUA template)	SPHN Projects
	Possibility that incidental research findings can be returned/reported back to the patient/study participant/citizen	Who/which institution decides if data can be used for research; what kind of consent possibilites are there for the specific data types?	Data are often pre-structured or quality-controlled by clinicians, clincial specialist or consortia. This effort needs to be considered, as well as the clincial scientific expertise of the latter stakeholders. They should be considered as collaborative research partners.	In the document DTUA, 3 scenarios are defined: 1. The RECIPIENT is the owner of the RESULT(S); 2. The RECIPIENT only is the owner of the Result(s) but the PROVIDER is granted a license on the Result(s) and/or receives a portion of the revenues from the commercialization; 3. The IP is jointly owned by the PARTIES (tbd, categories are first proposals).	Examples of SPHN Projects (first and second calls for proposals) effectively using the respective data types
	Possible	Hospitals; general consent or informed consent	none	1 or 2 or 3	SwissPKcdw, Create, PRIMA, SPO
	Possible	Hospitals; general consent or informed consent	none	2 or 3	SPO, PSSS, ImmunoRep, Frailty, SHFN
	Possible	Hospitals; general consent or informed consent	none	2 or 3	SPO, PSSS, ImmunoRep, Frailty, SHFN
	Possible	Hospitals; general consent or informed consent	Variable, potentially none, but more likely clinical specialists, consortia of clinical specialists	2 or 3	SOIN, IMAGINE
	Possible, after de-coding	Hospitals or PIs; general consent or informed consent	Clinical specialists, consortia of clinical specialists	2 or 3	SPO
	Possible, after de-coding, depends on intial specific consent	PIs; informed consent or legal basis (e.g. Transplantation, Cancer)	Cohort Consortia, PI	2 or 3	SACR
	Possible, after de-coding, depends on intial specific consent	Hospitals or PIs; informed consent or general consent	Cohort Consortia, PI	2 or 3	PRECISE, SHFN, Frailty
	Possible	Patients	none	1 or 2 or 3	
	Possible, after de-coding	Hospitals; general consent or informed consent	Clinical specialists, consortia of clinical specialists	2	SPO, SOCIBP
	Possible, after de-coding, depends on intial specific consent	PIs (depending on the DTUA/MTA); general consent or informed consent	Scientific consortia	2	PRECISE, PSSS, ImmunoRep
	Possible	Citizen	Citizen data, PI	1	
	Not applicable	Not applicable	Epidemiologist, consortia of clinical specialists	2 or 3	SACR

Appendix III: Table of Abbreviations

CSI
Clinical Semantics Interoperability

DCC
Data Coordination Center

DTUA
Data Transfer and Use Agreement

EC
European Commission

ELSI
Ethical, Legal and Social Implications

ELSIag
Ethical, Legal and Social Implications advisory group

EU
European Union

FOPH
Federal Office of Public Health

HRA
Human Research Act

ICPerMed
International Consortium for Personalized Medicin

IAB
International Advisory Board

IT
Information Technology

M
Million

MO
Management Office

MTA
Material Transfer Agreement

NAB
National Advisory Board

NSB
National Steering Board

PM
Personalized Medicine

PH
Personalized Health

PHI
Personalized Health Informatics Group

PHRT
Personalized Health and Related Technologies

RI
Research Infrastructure

SAKK
Swiss Group for Clinical Cancer Research

SAMS
Swiss Academy of Medical Sciences

SBP
Swiss Biobanking Platform

SCTO
Swiss Clinical Trial Organisation

SERI
State Secretariat for Education, Research and Innovation

SIB
Swiss Institute of Bioinformatics

SNSF
Swiss National Science Foundation

SPHN
Swiss Personalized Health Network

UH
University Hospital

WG
Working Group

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