PERMIDES Strategy Document

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Content

About PERMIDES and the Purpose of this Document

It is the aim of PERMIDES to strengthen the competitiveness and foster the innovation potential of Personalized Medicine as an Emerging Industry in Europe by providing key solutions for the reconfiguration of the biopharmaceutical value chain by establishing connections between biopharmaceutical SMEs and the ICT/software sector as an enabler of innovation in many industries. PERMIDES is providing a semantic online matchmaking portal (PERMIDES Platform), matchmaking and dissemination events that will allow biopharma enterprises to identify a suitable ICT partner matching the needs of the biopharma partner. Furthermore, biopharmaceutical SMEs collaborating with ICT partners can apply for a joint innovation project supported by an innovation voucher to tackle an innovation barrier in the value chain.

This document outlines the strategic focus of the PERMIDES voucher based funding system and the rational for developing the matchmaking platform based on the results of a series of European workshops involving biopharmaceutical and IT SMEs during the initial PERMIDES project phase.

Project Facts

Project Acronym:	PERMIDES
Project Title:	Personalized Medicine Innovation through Digital Enterprise Solutions
Project Reference:	H2020-INNOSUP-1-2015, Grant agreement no: 691546
Project Type:	Cluster facilitated projects for new value chains
Project Duration:	24 months from 01.09.2016 – 31.08.2018
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Web:	http://www.permides.eu/

Project Partners

- CyberForum e.V. (Coordinator) (Germany)
- Cluster for Individualized ImmuneIntervention (Ci3) e.V. (Germany)
- Oslo Cancer Cluster S.A (Norway)
- NCE Smart Energy Markets (c/o Smart Innovation Norway AS) (Norway)
- Oncotyrol Center for Personalized Cancer Medicine GmbH (Austria)
- IT-Cluster - Business Upper Austria OÖ Wirtschaftsagentur GmbH (Austria)
- intelligent views GmbH (Germany)
- NETSYNO Software GmbH (Germany)

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Background and Rationale for PERMIDES Project

It is the ambition of PERMIDES to accelerate the digitalization of biopharmaceutical SMEs in the field of Personalized Medicine, thereby reconfiguring the value chain and increase the competitiveness of the participating SMEs. In comparison to other industries (such as the automotive or other engineering-related industries), the healthcare and biopharmaceutical industry is substantially lagging in adapting novel digital solutions to accelerate processes and implement new business models. This is mostly due to the complexity of the product development process as well as regulatory, legal and cultural hurdles.

The digitalization of communication and workflow processes is changing entire value chains. Advancing Personalized Medicine in the digital age requires solutions to issues currently driving the IT and software sector, e.g. Big Data, machine learning, IT security, data protection and cross-enterprise collaboration. As cross-cutting industry, the IT and software sector is an innovation enabler in many industries providing processes and best practice solutions in diverse industrial and business environments.

Biopharmaceutical SMEs are faced with specific challenges when it comes to digitalization of their processes and developing towards “digital enterprises”, i.e. enterprises where all processes are digitized. While equipped with the leading scientific experts in the field, these SMEs are often stringently bound to their core developmental asset due to several factors. The financial scope of SMEs is often very limited and does not allow them to screen for potential providers of and to invest in customized support technologies like IT-systems (Lack of Funding). Furthermore, SMEs are often very small and their teams are composed of biopharmaceutical R&D experts strongly focusing on advancing their drug or diagnostics product candidates but with very limited outreach to experts from the IT sector (Lack of Interaction). In comparison to larger companies, SMEs are unable to maintain employees or even departments for support technologies such as IT solutions and they usually do not have the resources to keep track of major digitalization trends occurring now also in the biopharma sector (Lack of Know-how). In summary, this results in a lack of awareness, access and implementation resources for novel digital solutions in biopharma SMEs which is a significant threat for their competitiveness. State-of-the-art support technologies from the IT sector are increasingly required for successful innovation and market entry. This is of importance in the field of Personalized Medicine, where requirements for data management and data analysis exploded with the introduction of new life science technologies (next generation sequencing, metabolomics, proteomics etc.), and where requirements for data protection and privacy are a central issue.

According to a recent survey by Arthur D. Little and the Karlsruhe Institute of Technology (“Impact of Digital Health on the Pharmaceutical Industry”, 2014), by 2020, the business model of the Pharmaceutical Industry will be reshaped by Digital Health. Personalized Medicine will be increasingly driven by these novel Digital Health solutions. These developments transform existing value chains and create new ones. Digital Health solutions, therefore, will be the key driving force for advancing Personalized Medicine and the reconfiguration of the pharma value chain towards a Health Economy 4.0 approach.

At present, the Digital Health sector is largely dominated by US companies, including big players like Google, Apple, Amazon and IBM Health complemented by a rapidly growing and well-funded start-up sector. A recent study performed by RockHealth confirms a growing interest investors have in this emerging sector, and indicates that "Digital health funding in 2014 exceeded $4.1 billion, a total greater than that of the past three years combined. The $4.1 billion total represents a growth of 124 percent over last year's investment total." Europe can build on active innovation milieus in Personalized Medicine and ICT as represented in the PERMIDES cross-sectoral consortium and other differentiating factors like public health care systems, clinical biobanks, and national health registries (especially in the Nordic countries).

PERMIDES will strengthen industrial leadership in the EU and Associated Countries by making biopharma SMEs in the field of Personalized Medicine more competitive through a better integration of state-of-the-art IT solutions in their processes and products. Currently, this sector is lagging in the knowledge and integration of solutions that constitute digital enterprises. Advancing biopharma companies into digital enterprises holds considerable innovation potential, and this is what the PERMIDES activities will unleash.

General Conclusion on PERMIDES EU Workshops

The European series of PERMIDES regional workshops in total gathered around 100 participants representing biopharmaceutical, IT and bioinformatic SMEs as well as larger companies, medical university centers, healthcare networking organizations and technology transfer initiatives. Although this series of workshops aimed at identifying regional priorities regarding digitalization challenges of the biopharmaceutical value chain, it is now evident that there is no particular regional focus. Similar aspects of digitalization of the value chain are rather seen as the most challenging by the respective industry sectors of different European countries. In particular, three of the value chain challenges that were initially identified by the PERMIDES consortium and open for discussion during the workshops were regarded as high-priority challenges reflecting actual industry needs by the majority of the workshop participants. These most relevant value chain challenges are:

- **Data gathering and exchange**: access to broad and complete data in real time
- **Big Data Analytics & Machine Learning**: actionable insights from massive data sets
- **Regulatory compliance** of novel data storage and mining solutions

Although no significant difference between the different regions regarding specific value chain challenges was observed, the Norwegian, and judging from comments made by representatives from Nordic countries, the Nordic countries Denmark, Norway, Finland and Sweden seem to have a somewhat better developed and advanced healthcare IT infrastructure than Germany and Austria. One of the main reasons seems to be the excessive concern with data protection, e.g. in Germany.

SME Needs as Driver for PERMIDES Project

The overarching objective of the PERMIDES project is to support biopharma SMEs in the field of personalized medicine to overcome innovation barriers and reconfigure their value chain through linking with IT SMEs and the implementation of cutting-edge software solutions. To achieve this, during the PERMIDES Project Phase I, we strategically adjusted the PERMIDES work plan based on the output of our initial workshops and discussions with biopharma & IT SMEs. The adjusted PERMIDES work plan structure will:

1) Validate the concept and approach of this project with SMEs from the participating biopharma and IT clusters (via a series of workshops), leading to a need-based innovation voucher framework that has the potential to fulfil the objectives of this project. During these workshops the value chain challenges already outlined in the PERMIDES Project proposal were basically confirmed and further specified (see next chapter). Based on the typical development phase of biopharma SMEs (exploratory, preclinical and early clinical development stage) there was a strong interest and need for digitalization solutions addressing challenges regarding the gathering, exchange, analysis, quality and security of data. Furthermore, IT solutions for compliance with legal and regulatory requirements are of particular interest to biopharma SMEs. Since bioinformatics companies combine expertise from both sectors, understand the needs of biopharma companies and integrate novel IT tools and trends into their products and services they can be an important innovation driver for the digitalization of biopharma R&D processes.

2) Provide an infrastructure in the form of the PERMIDES platform for support of matchmaking as well as preparation and submission of voucher applications, raise awareness about digitalization challenges and opportunities, foster matchmaking between biopharma and IT SMEs and build links with the relevant regional Managing Authorities – all prerequisites for successful innovation projects. The PERMIDES Platform and Innovation Voucher Framework have been developed to address the needs of the biopharma SMEs and to lower the hurdles for interested companies to engage and benefit from the project. Based on the experiences around the European Workshops continuous awareness raising, active mobilization and individual support of biopharma SMEs will be key for the successful outcome of the Innovation Work / Voucher Framework of PERMIDES.

3) Widely disseminate an open call for funding vouchers, select the most promising applications, monitor the performance of the corresponding consultancy and innovation projects and conduct follow-up coaching.

4) Collect results and success stories from the consultancy and innovation projects and widely disseminate the findings to SMEs with similar challenges, policy makers at regional, national and EU level and the sector at large.

Increasing the Competitiveness of SMEs: Strategic Focus for the Innovation Voucher Framework

To validate the concept and approach of the PERMIDES project and to develop an industry need-based innovation voucher framework we organized a series of workshops with relevant stakeholders. The European series of PERMIDES regional workshops and the initial strategy workshop in Frankfurt (Germany) in total gathered more than 100 participants representing biopharmaceutical, IT and bioinformatics SMEs as well as larger companies, medical university centres, healthcare networking organizations and technology transfer initiatives. The workshops aimed at identifying and prioritizing digitalization challenges in the biopharmaceutical value chain. The analysis of the workshop results demonstrated that similar challenges and needs are prioritized by SMEs from the different European countries. In particular, the value chain challenges 1-3 initially identified by the PERMIDES consortium and discussed during the workshops were regarded as high-priority challenges reflecting actual industry needs by the majority of the workshop participants. See Figure 1 below for details:

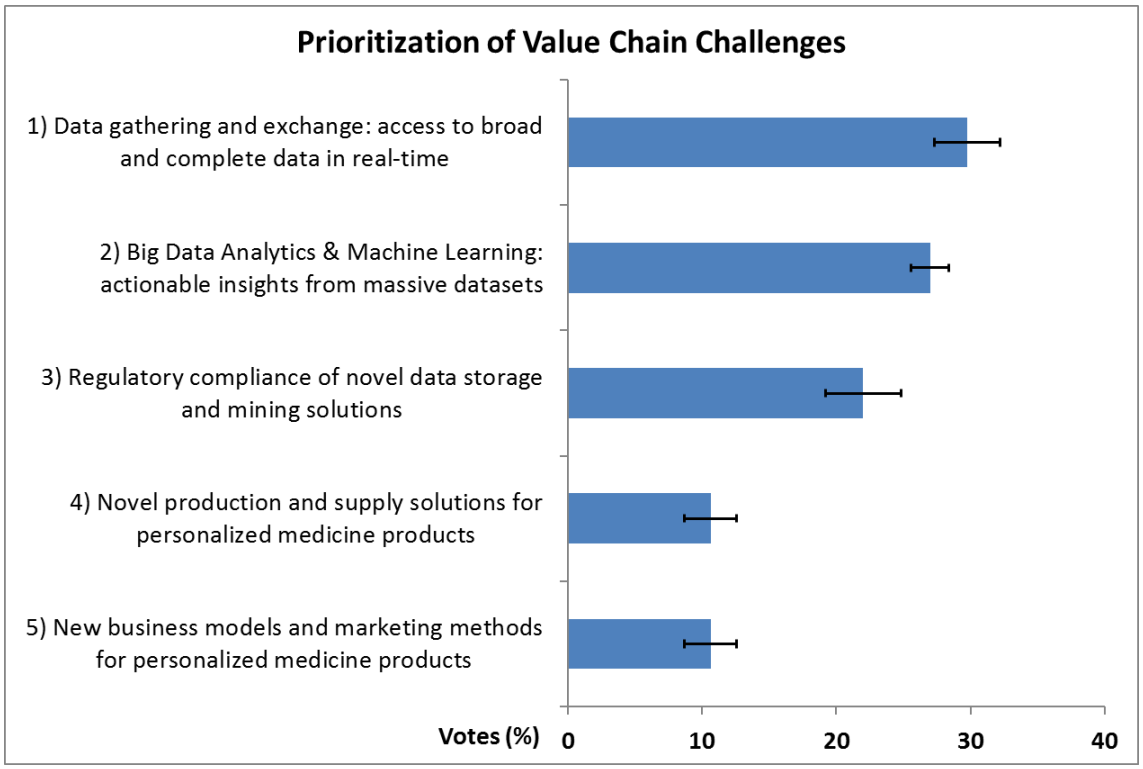

Figure 1. Prioritization of Value Chain Challenges by biopharma and IT industry representatives. In total 79 votes were casted. Error bars (SD) indicate deviations in voting collected during PERMIDES regional workshops in Oslo and Mainz.

Furthermore, our workshops identified which processes of the biopharmaceutical value chain and which digital technologies and trends are regarded as most relevant specifically for the SMEs. Figure 2 illustrates this in a word cloud

The workshops indicated that potential innovation barriers to be addressed by digitalization are mainly in the early part of the biopharmaceutical value chain, i.e. R&D processes from discovery to preclinical research and early clinical development. This represents a SME-specific point-of-view and has been expected because biopharma SMEs are typically performing early R&D programs rather than production processes and global marketing where they usually partner with larger companies.

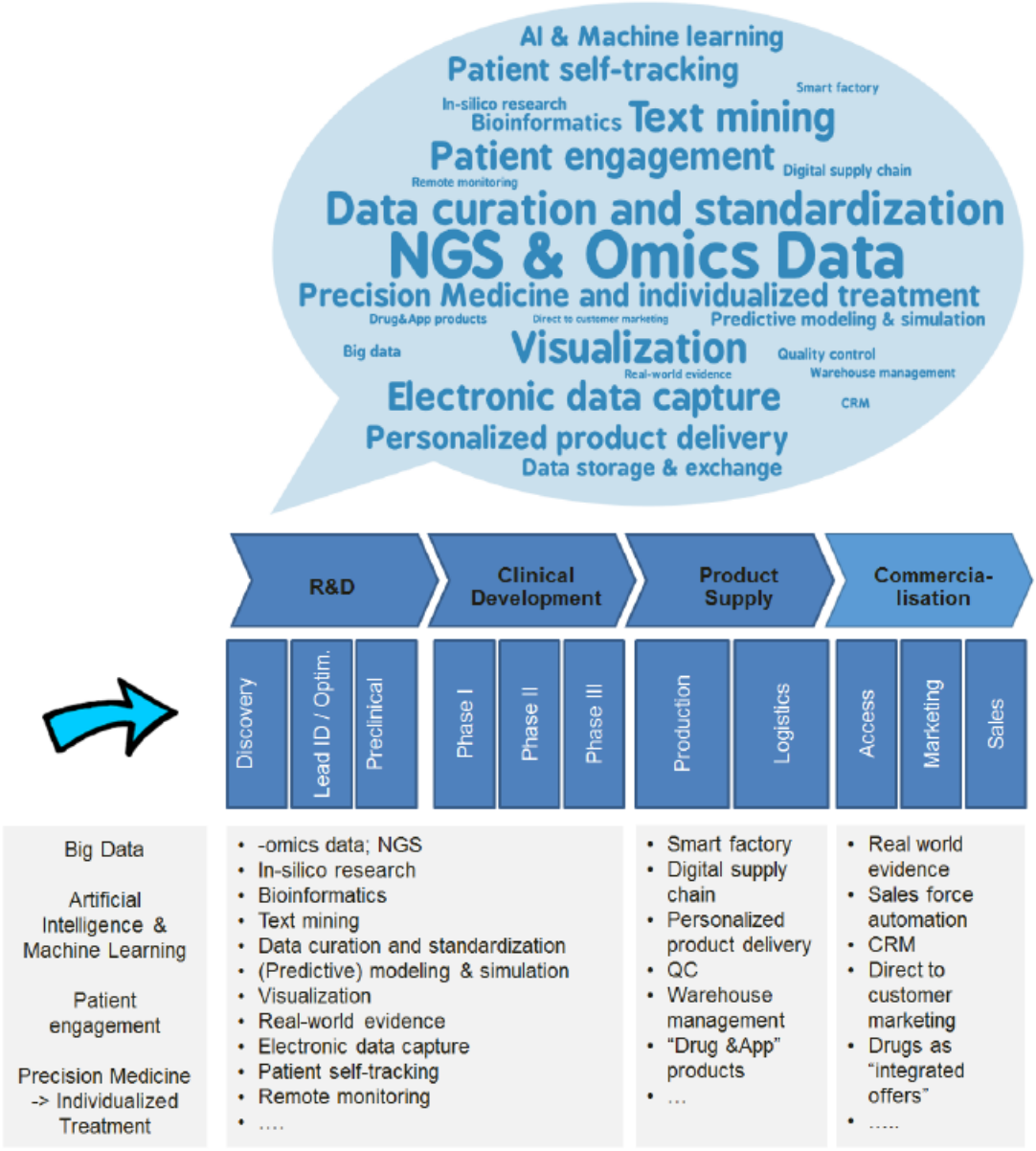

Figure 2. Digital technologies & trends in the biopharmaceutical value chain and their perceived importance shown as Word cloud representation. Results represent a total of 144 contributions collected during PERMIDES regional workshops in Oslo and Mainz. Word size is relative to the average of casted votes per topic in all workshops.

Prioritized Value Chain Challenges and Innovation Hurdles for the Voucher Framework

The PERMIDES workshops identified various challenges in the biopharmaceutical value chain that could be addressed in innovation and consultancy voucher projects. The following areas are regarded as most important and the described issues and solutions represent examples of what kind of topics should be pursued by PERMIDES funded projects.

Data Gathering and Exchange

- Conversion and standardization of the data across different research areas, clinical groups and laboratories is a common major challenge across the biopharma industry. The diversity of the data in the biopharma/biotech SMEs makes the automatic extraction and interpretation/visualization of the information next to impossible with the existing tools/formats. The IT industry can bring its advanced tools, like machine learning and annotation tools, to overcome the difficulties in handling various formats of data within the biopharma value chain.

- Exploiting external knowledge bases (e.g. existing scientific literature, patents, ongoing clinical trials, biobank data, etc.) more comprehensively via IT solutions to gain valuable insights for decision making and project planning is of large interest to the biopharmaceutical industry.

- Structured data acquisition especially in the context of clinical data is a major challenge. Access to clinical information systems for biotech and research companies is often a very difficult and long process if not impossible at all. The high security status required to protect patients' data is a barrier hampering data exchange with hospitals, while the providers of clinical information systems are reluctant to provide the required information for interfaces. Another major challenge in that context is the lack of standards in documentation. Still the individual admission notes based on verbal input and documented in pdfs (or similar) are state-of-the-art. No standard defines the way such admission notes are generated, making an automated data extraction nearly impossible. Thus, solutions for data standardization, structured data extraction and anonymization are highly desirable.

- Data Governance as in many fields is a problem in biopharmaceutical value chains. Managing the vast amount of complex data as used e.g. in the field personalized medicine can be possible if lean management systems that can scale down the complexity of the data can be developed. This is a challenge that needs to be solved to achieve sustainable business models. Furthermore, there is a gap in the logistics of data management in healthcare that can be filled with the help of the IT sector through the development of innovative tools, visualization and analysis software. Examples include tools that combine patient data, clinical trial data, diagnostic data,

production data and therapeutic data to gain insights on treatment regimens for diseases. In general, tools to combine data and ask different new questions would allow gaining new insights based on the already existing data.

- Social media are an interesting source of data relevant for healthcare ranging from epidemiology to quality of life assessment. Tools to efficiently and comparably assess and compare data extracted from social media are highly desirable.

- Digitalization can catalyse the development of new business models such as app-facilitated patient empowerment and direct pharma to patient marketing with potential to disrupt the industry represent excellent opportunities for biopharmaceutical SMEs. Educational programs and e-learning applications are suitable tools to advance interdisciplinary communication between biopharma and IT which is of major importance to drive this development.

- Technical solutions for transferring large amounts of data from mobile devices are needed. Here, challenges exist regarding technical storing aspects, as well as regarding standards for exchange / storing data.

Data Quality

- The analysis of acquired (external) data (clinical or research) is often hindered by the lack of reliable quality of the data. Different standards but also standard operating procedures in data sources lead to difficulties in generating homogenous datasets for analysis. This is a major innovation barrier since no automated quality control systems exist and a global standardization of data quality is unlikely. Especially in clinical trials, missing clinical values or absence of enough patient trails are problematic to make the final decisions on the efficacy of biopharmaceuticals or drug molecules. Still there is an extensive use of Excel sheets in clinical trial firms and clinics, and the complexity increases when multiple companies are involved in a trial. Data standardization and use of IT/software to ‘search’ and ‘analyse’ the clinical data can be immensely helpful in this sector.

- Data quality and data curation are of particular importance as there is a large variety of different data from different sources that needs to be integrated. Challenges exist regarding the digitalization and structuring of analogue content, e.g. handwritten or dictated notes. The availability of structured clinical data is an urgent need. Laboratory parameters and a few other clinical characteristics are often stored as structured data – depending on the clinical information software used. However, the documentation of clinical diagnosis and staging is still mainly based on verbal dictation followed by transcription into text and storage as PDF. Since standards for the verbal dictation are not even available, automated data extraction by artificial

intelligence or machine learning is not yet available. Apart from clinical data, heterogeneous software systems with specific data formats and qualities impair collaboration between researchers, public institutions and users. The development of systems to extract, combine and assure the quality of data from different data sources is thus highly desirable.

Data Analysis

- It is highly desirable to develop tools to gain actionable insights from external and internal data such as omics & biomarker data, scientific literature, clinical trial registries or patents which can provide decision support for R&D planning of biopharmaceutical SMEs.
- The analysis of complex molecular systems is still a major difficulty in structured biotech development concepts. While the transition from the trial and error principle to molecular targeted drug development is progressing, it is far from reaching a satisfying level. On one hand this is due to the highly complex biological processes, on the other due to the lack of molecular analysis systems or the acceptance of existing ones. Besides many others, analytical tools for image analysis and visualization of large and complex biological data are seen as important challenges that could very well be addressed by IT solutions.
- Healthcare is an interdisciplinary effort involving many contributors of different educational and specialization status. The facilitated and comprehensive communication of research data, clinical processes and results in between researchers, physicians, nurses, patients and other stakeholders requires support by the IT sector. Comprehensive data visualization including animations and augmented reality could contribute to solve the problem.
- The change of individual patients over time is a fact often neglected in personalized therapy solutions. IT-based systems allowing the modelling of such changes in advance could help to optimize development and treatment

Legal and Regulatory Requirements

- Data privacy and regulatory compliance issues are major hurdles to data access and sharing, especially since biopharma SMEs are performing their R&D projects in different countries. Main challenges exist regarding data protection during storage and transfer as well as regarding data privacy and anonymization. There seems to be an urgent need for support when it comes to certification/approval of digital processes that are used in a medical/therapeutic/clinical context.

- The legal aspects of data storage and exchange are a reason for the reluctance of many biotech companies to use potentially available support systems provided by the IT sector. National variations of the regulations are a challenge in a global business. In comparison to global pharma companies, SMEs usually do not have the resources for individual national solutions, while at the same time dependent on international activity. The required expertise for national and even more so for international activities often requires costly external expertise. Even IT-companies are challenged by unclear and heterogeneous legal and regulatory requirements. Computer systems assisting in the correct handling of data are lacking or are proprietary to large pharma companies, and as such are not available to SMEs. Therefore, the development of tools that ensure compliance from the very beginning such as a "digital compliance helper" is highly desirable.

- There is a need for changing certain certification processes. New technologies are sometimes dependent on the adaption of regulatory requirements, e.g. certain diagnostic tools allow the parallel processing of several thousand tests on different molecular alterations. For clinical use, each test would have to be EC certified individually which would take several months for each test representing a challenge that is currently not manageable. Therefore, support is needed to certify/approve digital processes that are used in a medical context.

Security

- Data Security is an inherent problem in the health sector at the global level due to the presence of different rules in different countries and regulatory bodies. Educating the relevant stakeholders is important especially in countries with a public health system. Secure data sharing and privacy is of utmost importance. Enabling data transfer between different actors & partners and across borders (e.g. clinical trial in Germany, sequencing in UK, drug production in Norway) would be a major step forward. According to PERMIDES workshops participants, the Nordic countries Denmark, Norway, Finland and Sweden seem to have a somewhat better developed and advanced healthcare IT infrastructure than Germany and Austria. One of the main reasons seems to be the excessive concern with data protection, e.g. in Germany.

Further to the scope and potential challenges that could be addresses by specific voucher projects, the workshops delivered valuable feedback on the general aspects of the PERMIDES voucher framework and its potential reach, as detailed below:

- **Communication**: According to both industry sectors it is of tremendous importance to mediate the communication between IT and Biopharma. A reoccurring problem seems to be for example the communication and technical interaction with hospital IT-departments, which is not always based on technical or regulatory facts. The PERMIDES platform is envisaged as an integrator and solution provider for digitalization of the biopharma industry in a broader sense beyond SMEs, e.g. also including larger ICT players, which aims to enhance the communication between both the IT and biopharma sector. In this context, it is interesting to note that in our experience companies from the IT sector were readily appreciating our workshop invitations whereas it was more difficult to mobilize biopharma companies to participate. This indicates that there is a need to raise the awareness for digitalization topics especially in the biopharmaceutical industry.

- **Influence on policy makers**: It is regarded to be of great importance that EU regulatory policy makers are made aware of the urgent need to unify the legal requirements regarding compliance of data security and exchange concerning the biopharmaceutical industry. Thus, working groups on regulatory issues (as they are common for example in the financial sector) are highly desirable, especially those focusing on regulatory aspects of the digitalization of processes of the biopharmaceutical industry. Furthermore, regarding the fact that some European countries have higher labour costs than other European countries might lead to imbalances when searching for an IT partner as a service provider in an innovation project giving a preference to low-cost countries due to the EU-wide funding limit of PERMIDES Vouchers. Therefore, it would be desirable if EU policy makers would consider a country-specific funding rate. However, lobbying on a political level is not considered as a task for PERMIDES itself.

Summary

During the initial PERMIDES project phase, we specified the challenges that biopharma SMEs in Europe are confronted with regarding digitalization. Our initial workshops and discussions with SMEs were an important first step to raise the awareness of the opportunities residing in novel digital solutions and to communicate the need for SMEs to move into this direction to maintain & increase their competitiveness in the future. During the initial project phase, main challenges spanning the entire value chain as outlined in the PERMIDES project proposal were basically confirmed and further specified. Thus, we aim at a call that attracts technology-wise broad proposals of collaboration projects between biopharma and IT SMEs addressing these value chain challenges by means of digitalization. Of particular importance will be digitalization solutions addressing challenges regarding the gathering, exchange, analysis, quality and security of data as well as solutions for compliance with legal and regulatory requirements.