BIO DEUTSCHLAND
Biotechnologie-Industrie-Organisation Deutschland e. V.

Position paper of BIO Deutschland

concerning big data applications in healthcare

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1. Summary

Big data – the analysis of large quantities of data – has become a top issue in the healthcare sector. The sector association of the biotechnology industry, the Biotechnologie-Industrie-Organisation Deutschland (BIO Deutschland), therefore welcomes the fact that German lawmakers, through the Law for Secure Digital Communication and Applications in Healthcare (e-Health Law), aim to seize the opportunities that the digital age offers the healthcare sector. Recognising the genetic diversity of humans is the basis for developing effective and advanced personalised medicine. This provides tailored treatment for individual people, but is also significantly more complex and necessarily based on highly differentiated knowledge that can be obtained only through the analysis of a vast amount of data. We therefore urgently need to develop new approaches to healthcare delivery, which can be achieved only through new discoveries in the digital healthcare sector.

Big data not only improves the quality of healthcare delivery, enhances healthcare efficiency and strengthens the patient's right to self-determination, it also creates added social value on a broad scale, particularly if big data solutions can help advance innovative research.

In 2016, studies on the potential of the digital healthcare sector – commissioned by the Federal Ministry of Health (BMG)[1] and the Federal Ministry of Economic Affairs and Energy (BMWi)[2] respectively – were

[1] "Weiterentwicklung der E-Health-Strategie" (Further Development of the e-Health Strategy), published in November 2016.
[2] "Ökonomische Bestandsaufnahme und Potenzialanalyse der digitalen Gesundheitswirtschaft" (Economic Stock-Taking and Potential Analysis of the Digital Healthcare Sector), published in May 2016.

published. These studies found that big data offers significant potential for improving research. In order to fully realise this potential, it is of critical importance that data protection laws be revised. Germany must be careful that its strict regulations and myriad restrictions do not lead to it squandering its position as an innovation location.

BIO Deutschland therefore calls for:

the **creation of statutory exemptions allowing for the processing of data for research and development (R&D) purposes**,

the **recognition of a more flexible purpose limitation principle** and

the **harmonisation of data protection laws**.

The aforementioned studies also discovered that a connected healthcare infrastructure (interoperability) has increasingly become a central prerequisite for the digitisation of actors involved in healthcare delivery. The current version of the e-Health Law leaves unanswered the crucial question of how to integrate medical data from the various information systems.

BIO Deutschland therefore advocates **making healthcare actors more connected through standardised cross-sectoral guidelines and the incorporation of bioinformatics experts** into the development of interoperability structures.

The isolated solutions that still prevail today create an environment where, for example, physicians in other fields or other clinics often cannot access important patient information, which they would need to make comprehensive decisions regarding appropriate treatment options. Here the electronic health card applications, the telematics infrastructure and the Big Data for Better Outcomes programme, which has received several hundreds of million euros of EU funding to promote distributed data networks, offer a path to more interoperability in healthcare. These applications have the ability to create an improved data basis – not only for service providers in terms of their delivery of healthcare to patients, but also for biotech companies in terms of their development of innovative and highly effective diagnostic and therapeutic methods.

BIO Deutschland therefore calls for a **swift introduction of all applications that go along with the electronic health card**, including the **involvement of biotech companies** in the associated decision-making processes, and for the **development of a strategy for gaining a better understanding of big data in healthcare**.

2. Introduction

In the field of healthcare, biotechnology is a driving force behind new active ingredients, methods and diagnostics. Rapid advances in basic and applied research in the past several years have facilitated the development of new therapeutic approaches for a whole host of different pathologies, including indications, for which there were previously no alternative treatment options. The necessary research and development

is, however, cost and time intensive. In Germany in 2014, biotech companies in the field of medical biotechnology spent 773 million euros[3] on research and development. The use of innovative methods to analyse research results, such as the rapid sequencing of DNA molecules (next generation sequencing), the investigation of proteomes with biochemical methods (proteomics) and big data analyses of health data, plays an increasingly important role here. Not only physicians but also biotech research companies need to have access to the broadest possible pool of data in order to gain a more precise understanding of medical processes and the interactions between drugs and to develop novel diagnostic methods and better therapies for treating patients. In this context, data on the entire course of a disease and further information on a patient's general health are required if biotech companies are to develop efficient and highly effective diagnostic and treatment methods. Big data analyses can be used, for example, to identify health risks so that available and suitable preventive measures can be taken in time. In the case of disease, big data analyses can contribute to the successful treatment of patients. This also leaves more time to establish a better physician-patient relationship, because "intelligent thinking" systems not only substantially reduce the workload of medical professionals but also improve their performance. The digital transformation makes health knowledge accessible, gives individuals control over their own health data and puts healthcare decisions in the hands of patients. Access to a larger pool of data not only makes it possible to enhance the quality of biopharmaceuticals developed in Germany but also cuts healthcare costs considerably. This helps strengthen Germany's position as a research location. However, further changes are needed to create a healthcare network that improves the medical care of patients while at the same time providing researchers opportunities to make progress and improvements that serve the interests of patients.

3. Examples of big data applications in the healthcare sector

Today there are still a number of diseases for which scientific research has not produced potential therapeutic options, because the underlying causes of a disease are often unknown. In the case of rare diseases – in Germany around four million people suffer from one of the 8,000 known rare diseases – it is especially vital to bring together all available information in order to ensure an exact diagnosis with detailed recommendations for modern and, where applicable, even personalised therapies. Yet what is also becoming increasingly important is the regular monitoring of disease progression in order to be able to describe characteristics more precisely and adjust the medication dosage to the current disease progression. This is only possible if individual patient data is documented, processed and compared in a standardised and anonymised (or pseudonymised) format, as, for example, is the case with mutation databases. These use real patient cases to link together genotypic, phenotypic and epidemiologic data. This makes it possible to analyse in a targeted way whether previously unknown mutations are pathogenic, whether known mutations need to be re-examined because of new clinical evidence or whether the medication dosage adjustments have a positive effect on disease progression. Such new discoveries can also lead to reduced costs in the healthcare system. A concrete example of database documentation of a mutation is the reclassification of a

[3] German Biotechnology Sector 2015/Facts & Figures; p. 19.

known mutation in the CTNS gene that causes cystinosis, a genetic metabolic disease. Cystinosis manifests itself between the third and sixth months of life, with symptoms including vomiting and weight loss. The affected children have a pigment deficiency, characterised by light blonde hair and a patchy depigmentation of the retina. They develop a renal insufficiency during the course of the disease. The infantile form of cystinosis usually leads to death by the age of ten. Based on a comparison of clinical-symptomatic data with the genetic characteristics of independent cases and existing literature, this mutation had to be reclassified from "likely neutral" to "likely pathogenic". As a result, patients whose cystinosis is caused by this very mutation can now receive appropriate treatment early on. Another example is the reclassification of a mutation in the BRCA1 gene, which is one of the genetic causes of breast cancer. Here a targeted and standardised comparison of existing data, from independent cases in different geographic regions, also clearly showed that a reclassification was necessary (from pathogenic to neutral), thereby having a direct influence on treatment options. In the future, the collection, standardised documentation, and comparison of international patient data will be the only way to deepen our understanding and knowledge of mutations and consequently identify the (genetic) causes of diseases – while also facilitating a personalised therapy at the earliest possible time. The diseases cited here illustrate just some of the benefits of big data in health research. Examples of statistically significant improvements made through big data analyses recently appeared in the journal *Nature*.[4] In the prevention, diagnosis and therapy of, in particular, widespread medical conditions such as respiratory and cardiovascular diseases and disorders of the nervous system, we also anticipate that big data analyses will lead to completely new research methods and solutions that enhance patient well-being.

4. Changes needed in German data protection law

While people often divulge data without giving it a second thought in today's digital world of social media and apps, there are still strong reservations about "officially" collecting and reusing data in the healthcare system. For data security reasons, there is an interest in data not being collected and used solely outside of Germany. The regulations currently in place in Germany, however, make data sharing between patients, clinics and researchers difficult.

4.1. Creation of statutory exemptions for data processed for R&D purposes

European and German data protection laws feature a strict purpose limitation principle: The processing of personal data, including pseudonymised personal data, must be compatible with the original purposes for which the data were collected. The EU's new General Data Protection Regulation (GDPR), however, gives German lawmakers a variety of options for better facilitating the processing of data for scientific research, particularly in the area of healthcare. European legislation recognises that the legitimate expectations of society for an increase of knowledge should be taken into consideration, that by coupling information from registries researchers can obtain new knowledge of great value with regard to widespread medical

[4] *Nature*, Vol. 536, 17 August 2016, "Editorial: ExAC project pins down rare gene variants"; "Human genomics: a deep dive into genetic variation", pp. 277–278; "Analysis of protein coding genetic variation in 60,706 humans", pp. 285–291.

conditions, and thereby enhance research results, and that for the purposes of the GDPR the processing of personal data for scientific research purposes should be interpreted in a broad manner, in order to take into account the EU's objective under Article 179(1) of the Treaty on the Functioning of the European Union (TFEU) of achieving a European Research Area.

German lawmakers should therefore exercise the discretion granted to them under Article 9 GDPR, particularly with regard to the processing of data for scientific research in the health field as permitted by the statutory exception that removes legal uncertainties and clearly regulates security and pseudonymisation measures. It is not sufficient to simply adopt the same text as the GDPR. In particular the safeguards addressed in Article 89, such as pseudonymisation and the specification of technical and organisational measures, should be defined with regard to scientific research in such a way that ensures legally certainty. Statutory exemptions for the processing of data for scientific research are absolutely necessary in order to promote Germany's status as a research location and to provide citizens with the best possible healthcare from a technological and legal standpoint.

Let's look now in more detail: First of all, Article 9(2)(g) GDPR gives EU member states the right to authorise the processing of sensitive data through a statutory exemption if the processing is necessary for reasons of substantial public interest and is proportionate to the aim pursued, and if such processing respects the essence of the right to data protection and provides for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject. Recital 52 of the GDPR reveals that European lawmakers had in mind here situations such as public health and the management of healthcare services or the processing of data for scientific research purposes. Recital 53 states that data should be processed for health-related purposes only where necessary to achieve those purposes for the benefit of natural persons and society as a whole, in particular for scientific research purposes or for studies conducted in the public interest in the area of public health. Article 9(2)(i) GDPR also gives EU member states the right to authorise the processing of health data through a statutory exemption if the processing is necessary for reasons of public interest in the area of public health or for ensuring high standards of quality and safety of healthcare and of medicinal products or medical devices. Moreover, Article 9(2)(j) GDPR enables EU member states to authorise the processing of sensitive data through a statutory exemption if the processing is necessary for scientific research purposes in accordance with Article 89 GDPR if the processing is proportionate to the aim pursued, respects the essence of the right to data protection and provides for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject.

Article 89(1) states that the processing of sensitive data for scientific research purposes is to be subject to appropriate safeguards for the rights and freedoms of the data subject, in particular through the obligation to apply pseudonymisation, provided that those purposes can be fulfilled in that manner, and through ensuring that appropriate technical and organisational security measures are in place. Moreover, EU member states may provide for derogations from data protection rights such as the rights of access, rectification and erasure in those cases where personal data are processed for scientific research purposes (Article 89[2]).

It is imperative that German lawmakers exercise these powers granted to them under the GDPR relating to the adoption of legal measures that facilitate the processing of data for scientific research purposes, even without the consent of the data subject.

4.2. Recognition of a more flexible purpose limitation principle

Under the current legal framework, data may be used only for purposes other than those for which it has been collected if the change of purpose is expressly permitted. Big data brings new approaches to research. It does away with traditional practices such as working hypotheses and focused studies. The opportunity provided by investigating large and diverse amounts of data lies primarily in the discovery of previously unknown correlations. This is due to the fact that prior to data usage, it is often not possible to define precisely the specific purpose of the research. Data also needs to be available over a long period time, because research projects into cutting-edge medical technology frequently take more than ten years to complete. Article 5(1)(b) and Recital 50 of the GDPR recognises a flexible purpose limitation principle for scientific research purposes, according to which the further processing of data in accordance with the provisions of Article 89, which is thus subject to appropriate safeguards (e.g. certain security and pseudonymisation measures), is to be considered lawful and compatible with the initial purposes. Recital 33 also provides flexibility with regard to the purpose limitation in cases where consent is given for scientific research purposes, because European legislation recognises that it is often not possible to fully identify the purpose of personal data processing for scientific research purposes at the time of data collection. German data protection law should therefore allow data subjects to give their general consent to certain areas of scientific research when in keeping with recognised ethical standards for scientific research.

4.3. Harmonisation of data protection laws

Today patient care in Germany cuts across institutions and *Länder* (states). Revisions to health data protection legislation at the federal and state level as a result of implementing the General Data Protection Regulation should be used to take into account this fact and to harmonise federal and state laws on health data protection. Due to the legislative powers set out in Germany's Basic Law, it is not possible to circumvent state laws on issues related to the healthcare sector. It would, however, be desirable for federal lawmakers to enact, in consultation with state lawmakers, framework legislation on health data protection that the respective state lawmakers can use as guidance.

Regulations on the protection of hospital patient data vary widely from state to state and are no longer suited to the times. This is especially true when it comes to statutory arrangements. While patient data collected in hospitals, for example, is normally covered by state hospital laws, the handling of such data in North Rhine-Westphalia is governed by a separate Health Data Protection Act. The provisions of the various state laws also contain substantive differences. While, for example, Section 24(8) of the Berlin State Hospital Act requires patient data to be deleted immediately upon completion of the task for which it was collected, Section 19(1) of the Hospital Act of Mecklenburg-Western Pomerania stipulates that access to patient data in medical records is to be blocked upon completion of treatment and deleted within a maximum period of 30 years. In view of the increasing digital interconnectedness in the healthcare sector, provisions such as Article

27(4) of the Bavarian Hospital Act fail to meet the requirements of the digitised healthcare sector: These include allowing hospital physicians to transmit patient data to other persons when doing so is required for scientific research and when the patient data remains in the hospital's "custody". Such a practice clashes with the patient's right to informational self-determination and is also detrimental to the patient's safety. Lawmakers at the federal and state level should therefore examine current data protection laws for ways to achieve a more uniform and flexible regulatory framework.

5. Improvement of systems interoperability

Interoperability is an important precondition for realising the opportunities provided by healthcare IT to enhance patient care. The digitisation of the healthcare sector also holds the potential to significantly improve the efficiency of prevention, diagnosis and therapy, and facilitates the development of more cost-effective processes. The data collected during medical research is not only complex, but is also derived from various sources – such as diagnostic devices, computer simulations, clinical studies or medical findings – and stored in diverse formats.

5.1. Creation of harmonised standards

In order to do justice to such complex structures, measures must be taken as part of the interoperability process to ensure that the implemented structures are expandable and upgradeable so as to be able to keep pace with technological advances. The structures must be designed in such a way that facilitates the participation of further healthcare stakeholders at any time. The e-Health Law emphasises the importance of not creating isolated solutions. This is a key point for biotech companies. To avoid this pitfall, it is necessary to ensure that the telematics infrastructure is interoperable with medical devices and other e-health and mobile health measurement and monitoring solutions, while also taking into account data protection. Therefore, there needs to be established an orderly, binding procedure for achieving interoperability, one concluded by a decision on which standards are admissible for which applications in the healthcare sector. When it comes to determining which standards to include in the interoperability register, it is necessary to define the inclusion criteria in a transparent way. These could be oriented on the policies of standardisation bodies. The uniform standards should undergo a review at regular intervals. Such a procedure would facilitate innovation and competition among service providers. A committee of experts – from the self-administration system, the pharma and biotech sectors, and IT solution manufacturers – should be established and empowered to coordinate the definition of uniform standards and to continually develop these standards further. Under the current legal framework, every standard can in principle be included in the interoperability register without any sort of review or even a decision on whether the standard is appropriate and practicable or whether it is recommended for other applications in the healthcare system.

5.2. Cross-sectoral integration of open interfaces

In order to improve the interoperability of the entire healthcare sector, horizontal competencies must be in place: Appropriate technical content related to medical, care, therapeutic, pharmaceutical and billing issues must be identified using a cross-sectoral approach. Building on that, the content must be designed in a

uniform way with regard to conceptual and technical aspects in order to facilitate communication across sectoral boundaries. The text of the e-Health Law remains in direct conflict with the objective of interoperability stated in the law itself. In the integration of open interfaces into IT systems (Section 291d of Book V of the German Social Code [SGB V]), there continues to be an explicit provision for sector-specific standardisation (vertical competencies) instead of requiring uniform cross-sectoral communication processes that could achieve interoperability across the entire healthcare system. The competencies defined in the legislation are oriented on the individual sectors and not along the pathway of patient care. The main objective of Section 291d(5) SGB V should be to require the relevant organisations to establish uniform cross-sectoral specifications in those areas where there are common characteristics, while allowing them to make specifications within the sectors only for special sector-specific areas.

5.3. Involvement of bioinformatics experts

From the very beginning, bioinformatics experts should be involved in ensuring the interoperability of healthcare IT systems. Only in this way can we be sure that the interests of patients and biotech and bio IT companies are protected, and that they can access data via the telematics infrastructure in a format and language that enables them to meaningfully use the data for their own purposes. It must also be ensured that the systems for bioinformatics applications can be integrated into the telematics infrastructure. With regard to the appointment of experts in accordance with Section 291e(5) SGB V, it remains, however, unclear which organisations are to be given consideration here. Clear specifications and understandable criteria are lacking as to how the organisations are to be selected. No organisation is entitled to be included nor has the right to make proposals. Criteria for the required qualifications of the experts are also not specified, nor is there an obligation to define such criteria.

6. Swift introduction of electronic health card applications

In order to ensure that insurance holders receive the best possible healthcare, all electronic health card applications must be introduced as swiftly as possible. Medication regimens, X-rays, etc. could be a first step towards this goal, but further medical applications, particularly the safety monitoring of pharmaceutical therapies and electronic patient records, must follow closely thereafter. These applications enable insurance holders to obtain information about their health status and give service providers access to the best possible data during healthcare delivery. The stored information can also significantly help biotech companies in their efforts to develop innovative and highly effective diagnostic and therapeutic methods. When introducing electronic patient records, it is important to make sure that the standards used are compatible with other systems – so that patients can freely and independently access their data.

6.1. Electronic patient records

The e-Health Law lay downs that, by the end of 2018, conditions shall be created enabling patient data from already available applications and documentation, such as emergency data or medication regimens, to be made available to patients in electronic patient records. Such e-records will then give medical practitioners access to this important health data. The e-Health Law, however, does not provide for the possibility to give

patients control over their entire medical records. They are granted only limited power to manage their data independently and to make such data available to physicians or other medical professionals during standard care. According to a representative survey by the digital industry association Bitkom, 87 percent of Germans want to have access to health data such as test results, X-rays, etc. Yet, irrespective of this fact, patients lack interfaces to the telematics infrastructure, which means they have no way to access information such as electronic correspondence. We therefore call for the creation of an open interface to the telematics infrastructure so that patients can freely and independently access their data. Further applications, such as radiological results, laboratory parameters and vaccination records, should be integrated into electronic records in successive iterations.

6.2. Incorporation of biotech companies in decision-making processes

When developing the technical concept of the telematics infrastructure and of the data records relating to the electronic health card, it is particularly important to ensure that biotech companies have not only secure, easy and reliable access to the corresponding health data but also that such data is available in a format suitable for the aforementioned purposes. To make sure this is the case and to enable biotech companies to bring their expertise to bear in the electronic health card project, companies in the biotech sector must be involved in the relevant decision-making processes. Because patients' health data is particularly sensitive, it is imperative to avoid data leaks due to hacking, manipulation or inadvertent loss of data.

6.3. Inclusion of the right to access for research purposes in SGB V

In order to provide effective support to research companies, including those in the biotech sector, it is furthermore necessary that SGB V be amended to give service providers and researchers a legal right to access for medical and biotech research purposes. Companies are barred from accessing such data under the current arrangements of the electronic health card. Instead, only those service providers specified in Section 291e(4) and (5a) SGB V and the insurance holders themselves can access the data stored on the electronic health card. In order to achieve the research objectives of the EU's General Data Protection Regulation and Article 179(1) TFEU, a specific provision is needed to clarify under which conditions the data specified in Section 291a(3) SGB V may be released, for example, after having undergone pseudonymisation.

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This position paper was prepared by BIO Deutschland's Working Group on Bio IT and Big Data.

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As the sector association of the biotechnology industry, **BIO Deutschland** has set itself the objective of supporting and promoting the development of an innovative economic sector based on modern biosciences in Germany. The Berlin-based association currently has over 330 members. **Dr Peter Heinrich** is Chairman of the Board of BIO Deutschland.

BIO Deutschland's supporting members and partners are **Abbvie, Avia, Bayer Pharma, Biotest**, **Boehringer Ingelheim Pharma, Celgene, Clariant Produkte (Deutschland), CMS Hasche Sigle, Deutsche Bank, EBD Group, EY, Isenbruck │ Bösl │ Hörschler, Janssen, KPMG, Merck, MiltenyiBiotec, MorphoSys, PricewaterhouseCoopers, Qiagen, Roche Diagnostics, Sanofi-Aventis Deutschland, SAP, Thermo Fischer, Vertex** and **VWR.**

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