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Standardization in biobanking – between cooperation and competition

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Abstract: This article presents the current situation of German biobanks and shows future fields of action in the European and international context on the basis of upcoming legal and normative challenges. It gives an overview of the development of the international biobank standard ISO 20387 and the commitment of German biobank experts in the ISO committee TC276. Less attention than the biobank standard per se has so far been paid to the basic mechanisms by which standards are developed and the potential of their application and accreditation. In this sense, this article deals with the motivation for active participation in standardization projects. We discuss the status of ISO 20387 as a conformity assessment standard and the consequence of accreditation as a performance monitor.

Keywords: accreditation; biobanks; certification; ISO; ISO 17025; ISO 20387; Regulation on In Vitro Diagnostics (IVDR); standardization.

Biobanks – status quo

Biological resources are regarded as essential raw materials for the promotion of biotechnology, human health and research and development (R&D) in the life sciences. Through the use of biological resources, genomics, proteomics and molecular diagnostics have made unprecedented progress in the last decade, contributing to a better understanding of the pathogenesis and epidemiology of various diseases of global importance. The development of genomics platforms, molecular imaging and bioinformatics will enable significant progress toward personalized medicine [1].

Modern medical research is based on precisely defined study collectives with high-quality samples and data, compiled from various biobanks and bioclinical studies. To make such research possible, the collection, processing, storage and management of data and biosamples in existing biobanks must be harmonized. The collection of biosamples and their preparation for storage in biobanks is a complex process in which the activities of many actors must be seamlessly interlinked. A high degree of automation through robotics facilitates sample preparation, increases sample throughput and leads to consistent process quality. The prerequisite for automation is the use of standardized compatible components [2].

The large number of biobanks worldwide results in a high degree of heterogeneity with regard to the available infrastructure, information technology (IT) components, methods used and human resources.

It is still not easy for researchers to use the “treasures” of biobanks: The samples are too different in their quality, type of pre-treatment, storage, data documentation and data protection. Despite increasing awareness, overarching and uniformly binding requirements are still inadequate at present. In addition, difficult questions often arise for later utilization [2, 3].

In Germany, the first successes in terms of harmonization through cooperation between existing biobanks are visible. The German Biobank Alliance (GBA) was founded in 2017 and was joined by other biobanks in 2019. The German Biobank Node (GBN), a national node at the Charité, bundles all activities and cooperates successfully at the European level with the European Biobanking Research Infrastructure (BBMRI-ERIC) in order to further expand Germany’s role in international biobank-based research. Local biobanks that have focused their sample and data collections on specific issues are networked via a common IT structure, pool their expertise and make their biomaterial samples available throughout Europe through a federated sample search [4].

Standardization can make an important contribution to solving these tasks. GBA experts are actively involved

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in various standards-setting bodies, e.g. in the Medical Standards Committee "Quality Management in Medical Laboratories" in the European Committee for Standardization (CEN), in TC140 "In-vitro diagnostic medical devices" and in the Technical Committees TC212 "Clinical laboratory testing and in vitro diagnostic test systems" and TC 276 "Bioresources and Biobanks" of the International Organization for Standardization (ISO). The European collaborative project SPIDIA (www.spidia.eu) collects experimental data to identify the critical steps of sample collection for in-vitro diagnostics. If the influences of the sample collection on the result of the analysis planned subsequently are known, these can be minimized in order to achieve reliable results. The technical ISO standards for pre-analytics published in 2017 are based on the results of this project. From now on, these standards apply to users, developers and manufacturers of in-vitro diagnostics, including biomedical research institutions and biobanks as well as supervisory and approval authorities, as the state of the art in science and technology [5–7].

Fields of action

The development of translational medicine requires close cooperation in all phases of the development process – from basic research to application. It can therefore be assumed that potential project partners of a biobank are located in strictly regulated areas. The European Union (EU) Regulation on In Vitro Diagnostics (IVDR) and the new European Medical Device Regulation (MDR) replace the existing medical device directives. The IVDR addresses the entire in-vitro diagnostics market in the EU: from development to market surveillance, to application. It thus addresses manufacturers, importers, users as well as notified bodies and national authorities. It harmonizes the legislation governing the placing on the market and putting into service of in-vitro diagnostic medical devices and their accessories on the Union market. In-vitro diagnostic medical devices require specific legislation separate from other medical devices, in particular as regards risk classification, conformity assessment (CA) procedures and clinical proof. The horizontal aspects of the two regulations have been aligned. The IVDR sets high standards for quality and safety, inter alia by ensuring that the data obtained in performance studies are reliable and that the safety of study participants is protected [8]. The IVDR thus greatly increases the requirements for the conduct of necessary clinical trials. Overall, more attention is being paid to clinical data. However, the regulatory framework for the collection of clinical data is becoming more stringent [8].

An EU regulation is issued by the EU Commission and must be applied as European supranational law within a specified period of time. IVD manufacturers have a transitional period until 2022 to implement the requirements of the IVDR for their new and existing tests and to obtain CE marking according to the new regulations. For in-vitro diagnostics, a performance evaluation including clinical data must be carried out from then on at the latest. The aim is to demonstrate clinical safety, performance and a positive risk-benefit ratio for the designated and intended use of in-vitro diagnostic medical devices through performance evaluation. As under the In Vitro Diagnostic Directive 98/79/EC (IVDD), manufacturers must prove within the framework of the CA procedures that the requirements have been met. Type and scope of the CA procedures depend on the classes into which the products are classified. Authorities and notified bodies check this as part of the approval process.

However, some risks only become apparent in the course of daily use. Detailed requirements for a post-market surveillance system are therefore described in the IVDR (Articles 79–81, Annex III). These are almost identical to the requirements of the MDR, but differ with regard to the post-market performance follow-ups (PMPFs) to update the performance assessment. In principle, the focus is on ensuring clinical proof. Post-market surveillance includes the collection of all kinds of significant information from practice [9] (https://www.johner-institut.de/blog/regulatory-affairs).

The scientific validity must be proven, e.g. by current scientific literature. The assignment of an analyte to a specific clinical area or physiological condition (Art. 2, 38 IVDR) as well as the analytical and clinical performance must be continuously confirmed, for example, by participation in interlaboratory comparisons and PMPF studies. Part B of Annex XIII of the IVDR describes this with regard to the specific requirements for performance and documentation.

In the PMPF, both safety and performance data as well as scientific data are proactively collected to answer relevant safety or performance questions.

Scientific validity, the assignment of an analyte to a particular clinical or physiological condition (Art. 2, 38 IVDR) and analytical and clinical performance must be evaluated. The evaluation needs to be updated regularly.

The new regulations on market surveillance, vigilance and registration will also apply to "old products" from 2020 during a 4-year transitional period. Existing gaps must be closed by clinical studies or observational

studies. MDR also focuses on market observation and post-marketing clinical follow-up. The introduction of the In Vitro Diagnostics Regulation 2017/746 and the associated EU-wide standardization of approval procedures for clinical trials presents manufacturers with major challenges [10]. Manufacturers generally cite internal expertise in the areas of regulatory affairs and quality management (QM) as gaps. Twenty-five percent of manufacturers collect data but 58% see gaps in the collection of clinical data and 17% do not know exactly what is required of them. Many lack a precise plan. Companies fear significant additional burdens and need new partners to meet the challenges. Industry associations and interest groups are already advocating greater public support for clinical trials [9, 11, 12] (https://institutes.kpmg.us/content/dam/institutes/en/healthcare-life-sciences/pdfs/2018/the-race-to-eu-mdr-compliance.pdf).

Extensive sample and data collectives are required. Modern biobanks recommend themselves as reliable cooperation partners. The standardized documentation and determination of the sample quality and characteristics prior to the storage of samples in the biobank is absolutely necessary in order to meet changing requirements in the field of research and qualification of in-vitro diagnostics. Thus, the biobank can provide support here as a direct study partner and by prospectively building up relevant sample collections. As studies are usually carried out under everyday conditions, biobank experts are required both as mentors during the study planning phase and during the qualification of study personnel with regard to sampling, and also within the framework of quality monitoring during the course of the study. The analysis of suitable biomarkers that correlate with critical process steps of sample preparation allows the characterization of samples with respect to already recognized quality parameters. A uniform code, such as the standard PREanalytical Code (SPREC), documents the quality criteria in a standardized manner [13]. The introduction of a binding quality assurance concept can ensure the provision of larger collectives of the same quality in a high-performance network [2, 14].

Biobanks are actively meeting these challenges throughout Europe and are supported by various umbrella organizations. In this context, the GBN aims to create a national biobank network in which the participating partners guarantee the consistent provision of services. The application of international standards makes an important contribution to interoperability and sustainability [2]. For this reason, the GBA has defined and published specific technical requirements for its cooperation based on the requirements of internationally available standards. In the European sample portal BBMRI Directory, certificates of competence of the listed biobanks are deposited and searchable sample collections are labelled with regard to the standard methods used for pre-analytics [15]. A voluntary audit programme to assess the quality management system (QMS) of the GBA partner biobanks was launched in 2018 and helps the partner biobanks to implement the requirements of ISO 20387 on a site-by-site basis and checks compliance with the applied standards.

Further fields of action for biobanks result from the advancing digitalization. Future interactions require the combination of diverse and complex data sets [16]. The aim of the Medical Informatics Initiative funded by the Federal Ministry of Education and Research (BMBF) is to expand the networking of health data and thus improve their usability.

Registries, cohort studies and data repositories, as well as research projects related to these sources rely on procedures to ensure data quality [17]. As at the level of sample quality, a standardized, i.e. generally applicable, QM and quality assurance concept is also necessary here. Here, too, standardization can define requirements and set the framework for action. At the national level, the Technology and Methods Platform for Networked Medical Research (TMF e.V.) has provided appropriate recommendations and a set of self-assessment indicators for various types of empirical research projects with its guideline on data QM [18]. ISO/IEC 27001, published in 2013, aims to bring information security under management control as part of the ISO/IEC 27000 family of standards [19]. Organizations meeting the requirements may be certified by an accredited certification body upon successful completion of an audit. Other standards in the family of standards contain additional guidance on certain aspects (e.g. management of information security risks, ISO/IEC 27005).

The complex framework conditions with regard to normative and qualitative requirements represent a major challenge for all involved instances. Every biobank must assess its risks and set up appropriate processes based on its user needs and resources. The proof of applied standards can make the CA much more efficient.

Standardization is a shared responsibility

Although the importance of standards is generally undisputed, the process of standardization has received little attention in the academic biomedical research community to date. In addition, research, technology transfer and

application are often poorly linked. On the other hand, the effective, economic usability of the results is increasingly in the foreground, especially in publicly funded research projects. Standardization activities are recognized as activities to disseminate the results of research and innovation, in addition to publications and patents.

In the following, we would like to focus on the mechanisms for creating standards and their effects. Standardization is rarely a smooth process. It brings interests into conflict, yet it is a prerequisite for any form of cooperation. Every form of interaction is to some extent based on unification, on generic terms and clearly defined meanings, without which meaningful communication and exchange are impossible. The process of standardization has always been a central component of transnational and transcultural exchange. In Europe of the late 18th century, standardization was systematized for the first time. Its success was largely due to the political climate and the emerging internationalization and globalization. Germany professionalized standardization in 1917 with the founding of the Standards Committee of German Industry (NADI). The first DIN standard (DIN 1 taper pins) was published in 1918. Perhaps the most significant development in standardization today is the move toward standards designed to ensure compatibility between products, services or processes. Compatibility has two aspects, on the one hand the interchangeability and on the other hand the combinability of components. This change is becoming increasingly important, especially in large networks. Modern technologies are based on functioning compatibility. Applied to the context of biobanks, we speak of networks and interoperability. Scientific studies on the economic aspects of standardization clearly show that the network effect causes a loss of benefit outside the defined standards [20]. Standards support the tendency toward the formation of natural monopolies. Particularly in networks, the legal and factual binding nature of standards must be taken into account. On the one hand, innovations can only unfold their social benefits if they are widely disseminated. On the other hand, competition law aspects and the distribution of property rights pose challenges. Government regulations and legislative procedures are increasingly time-critical and are hampered by a lack of technical competence. The Gene Diagnostics Act lacks, for example, regulations on the handling of genetic samples and data in science and research. Moreover, politicians do not always see the necessity of a legal regulation, e.g. party proposals to examine (SPD) or establish (Greens) a biobank law were rejected in the past. However, the introduction of biobank secrecy, the guarantee that samples will be earmarked for a specific purpose, the anonymization of personal data and the prohibition of third-party research on samples and data of people who are not able to give their consent are regulatory objectives of the government [21]. This results in largely general legal requirements. Standards or guidelines cannot replace legal or regulatory requirements, but can usefully supplement or even close existing gaps. In Germany, standardization is the self-governing task of industry. The German Institute for Standardization (DIN) and the Competence Centre for Electrotechnical Standardization in Germany (DKE) are institutions recognized by politics, industry and society. DIN is a non-profit association, which is essentially financed by the sale of standards and services, project funds from industry, membership fees and project-related funds from the public sector. The interested parties represented are non-governmental organizations, companies, associations as well as science and research. State participation in DIN's national standardization processes has been contractually agreed since 1975.

In addition to participation in standardization committees, the government and state administrative authorities also use other opportunities to exert influence on the creation, dissemination or implementation of standards. Since 1985, the European Commission has applied its own procedure for the use of results at the European level, the "New Approach". Within the framework of product regulation and CA, only general requirements are made, e.g. for the safety of products that can be fulfilled in different ways, whereby conformity to European standards is considered sufficient to assume compliance with the requirements of EC directives [20]. In connection with the introduction of the IVDR/MDR, it should be mentioned that the EU Commission expressly calls for the application of standards and reserves the right to define so-called "common specifications" if it is of the opinion that harmonized standards are lacking or insufficient. Articles 105 and 106 of the MDR describe the desired cooperation of expert committees and specialist laboratories in the development of standards, common specifications and scientific and product-specific guidelines within the framework of the "Medical Devices Coordination Group" (https://www.johner-institut.de/blog/regulatory-affairs).

With regard to the influence of the Federal Government on the priority of processing standardization applications with public interest, the contractual agreements even go beyond the pure participation character [22]. The research policy guiding principle of the EU Commission "Open to the World" aims at common solutions for social challenges. Since 1984, EU Research Framework Programmes have been created for this purpose, which are continuously growing in terms of time and money. The

EU framework programme for research and innovation "Horizon 2020", with a volume of almost €80 billion, is currently the world's financially strongest and explicitly takes into account the growing importance of innovation. The aim is to create sustainable growth in Europe. The focus is on networking between science and industrial research. International, transdisciplinary cooperation and the sharing of knowledge, methods, infrastructures, personnel, data, etc. are seen as "European added value". Important partner countries are the USA, Canada and Japan. The Health, Demographic Change and Wellbeing Work Programme highlights the invaluable value of the population and patient cohorts already collected worldwide, including well-characterized clinical trial cohorts. The program sees a major challenge in increasing the degree of integration and networking in order to optimize the use of these resources. Mapping the cohort landscape in Europe and major international initiatives, integrating metadata on intended use, coverage and measurements and identifying the best strategies for cohort integration, taking into account relevant ethical aspects, are on the top of the agenda [23–26].

The establishment of ISO TC 276

In 2015, the United Nations (UN) drew up an ambitious 15-year plan to tackle some of the world's most important problems. Agenda 2030 for Sustainable Development is a programme of action for people, the planet and prosperity signed by the governments of the 193 UN member states. It comprises 17 sustainable development objectives (SDGs) in a comprehensive action programme. International standards provide effective tools to support organizations and companies wishing to participate in meeting this challenge and contribute to achieving sustainable development (https://www.unric.org/de/) [27]. ISO, the worldwide association of national standards bodies, classified biotechnology as an innovative field with high standardization potential as early as 2011. In order to identify possible standardization and certification activities, to derive needs for action and to initiate corresponding standardization activities, possible standardization projects were concretized in the international ISO workshop "Standards for Biotechnology" [28]. The International Technical Committee ISO/TC 276 Biotechnology was founded in December 2013. Almost 50 experts from 15 countries came to Berlin for the inaugural meeting in December 2013. Initially, five working groups were set up and a business plan formulated. The ISO/TC 276 is intended to ensure that the standards developed in its area of responsibility correlate with relevant international, national or regional legal or regulatory requirements or guidelines. The work of ISO/TC 276 is mirrored at the national level by the DIN Biotechnology Working Committee (Figure 1. ISO Working Groups and DIN Mirror Committees) [29]. GBA experts have been involved in this national committee since 2014 and in the international expert committee of Working Group 2 (WG2) Biobanks/Bioresources of ISO TC 276 since 2015. International standards are prepared by ISO technical committees. Any member interested in a subject (e.g. international governmental and non-governmental organizations) for

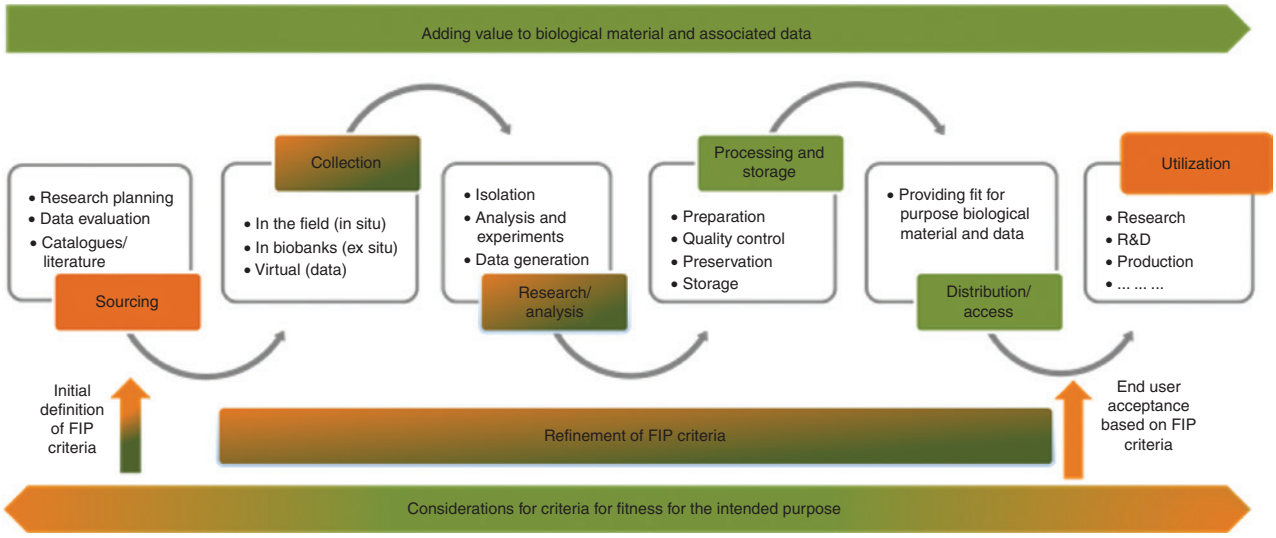

Figure 1: Main functions of a biobank or biobank process.
Source: Dunja Martin, 2019.

which a technical committee has been established has the right to be represented on that Committee [30]. DIN, as a state-recognized organization active in the Horizon 2020 funding programme with regard to the link to European standardization and standardization projects expressly requested therein, heads the secretariat of the TC. Cooperation with DIN was included in the GBA work programme.

The development of the biobanking standard ISO 20387 in TC 276

The development process of a standard is multi-stage and typically begins with identifying the needs of interested parties. The strategy for the development of a standard or a series of standards is derived from this. As biobanks offer a wide range of functions and activities, common needs are identified first. The definition of "quality" should be consistent with the biological material and related data, both of which must be made available for research and development of adequate quality. The quality delivered depends on the type of biobank and biological material, which may be a well-characterized sample, sample history or other definitions related to the biological material and associated data. Ultimately, this definition corresponds to proof of suitability for the intended purpose. The biobank standard ISO 20387 follows this principle of "suitability" for the intended.

Figure 1 illustrates the main functions of a biobank (collection, processing, storage and distribution) based on the life cycle of the biological resource. The identified main functions describe the value chain of the biological resource and the associated data outside and inside a biobank. The orange elements represent main functions that are usually performed by the user of a biobank or biological resource and the associated data, while the green elements represent classical main functions of a biobank. Mixed color elements can be assigned to both the biobank and the user.

Biobanks vary greatly in size and focus worldwide. Some biobanks are part of a conformity assessment body (CAB), e.g. a laboratory or an inspection body, and carry out extended activities such as analysis and inspection. These considerations influence decisions regarding the development of standards. A broad spectrum of biobanks should be involved in the development of the standard. The diagram in Figure 2 illustrates the main functions of a biobank (collection, processing, storage and distribution) based on the life cycle of the biological resource. Three CA guidelines can be derived from the identified functions and activities that describe the value chain in a biobank (see Figure 3).

- Technical competence (ability to achieve a certain result)
- Establishment of a QMS as a set of interrelated or interacting elements for the formulation of quality guidelines and objectives as well as quality assurance processes
- Requirements for biobanks to ensure that materials, products, processes and services are suitable for them.

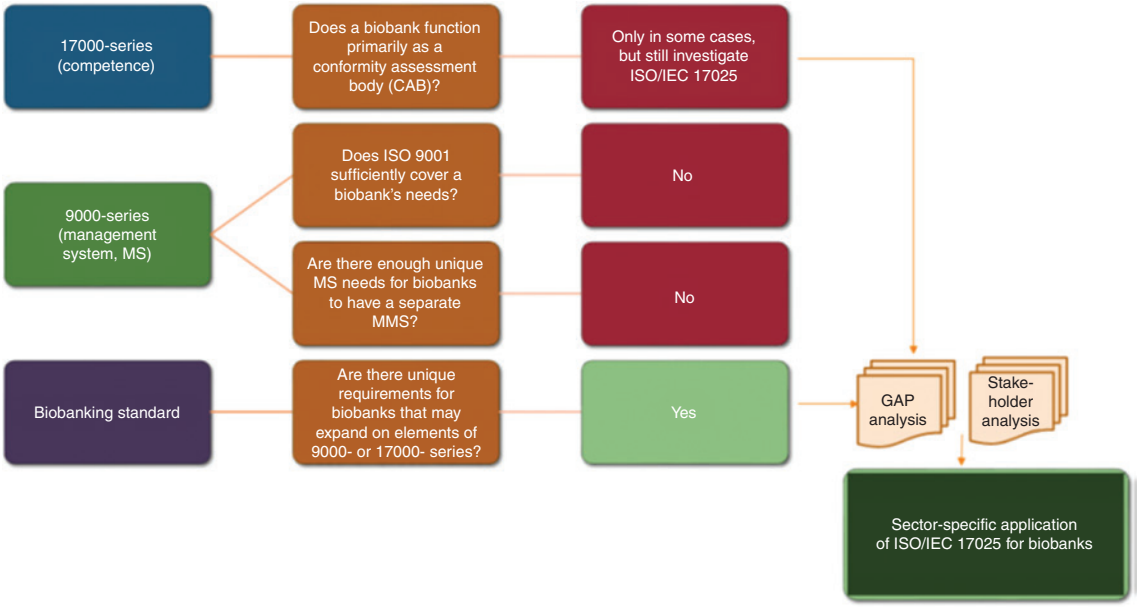

Figure 2: Schematic representation of the derivation of the ISO 20387 standard [31].

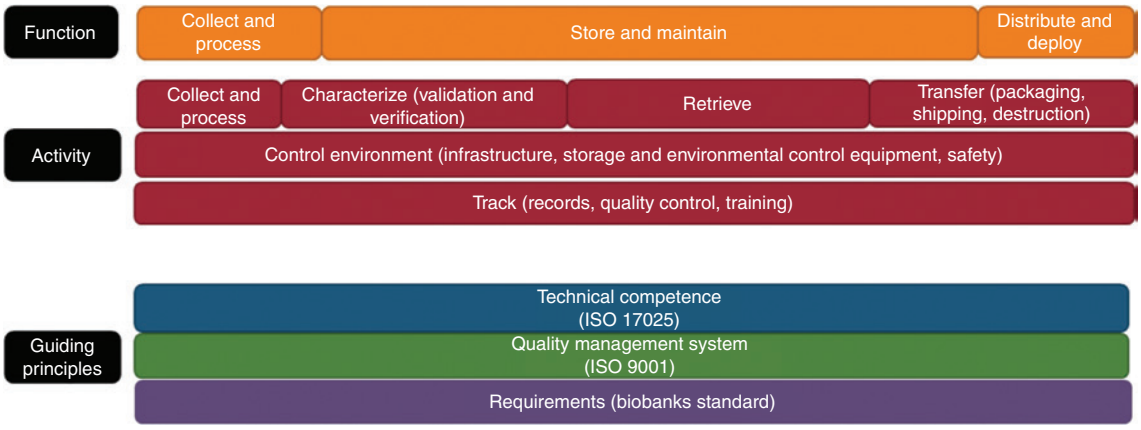

Figure 3: Main functions of a biobank as the basis of the life cycle of the biological resource [32].

ISO 20387 lays down general requirements for the competence, impartiality and consistent operation of biobanks, including quality control requirements. It applies to all biobanks of biological material from multicellular organisms (e.g. humans, animals, fungi and plants) and microorganisms for research and development and can be used by biobank users, regulatory authorities, organizations and systems using peer assessment and accreditation bodies. It shall not apply to biological material intended for the production of food/feed, to laboratories carrying out analyses for the production of food/feed and/or for therapeutic purposes [33].

An essential part of the discussion on a corresponding classification of the new standard for biobanks was the question of whether one should concentrate on a QMS (comparable to a specific interpretation of ISO 9001) or on competence assessment (standard of the ISO 17000ff series). Experience has already indicated the need for a combined approach. The gap and stakeholder analysis carried out by the expert panel confirmed that elements of the ISO 9000 and 17000 series had to be combined and extended to include specific biobank requirements. The starting point for further activities was the fourth meeting of ISO/TC 276 in Washington, DC, in 2016. After discussion with the International Council Committee for Conformity Assessment (ISO/CASCO), it was decided to develop an ISO/IEC 17025 sector application for CA. This means an industry-specific application of ISO/IEC 17025 supplemented by requirements and recommendations for biobanks. Most of the existing formulations of ISO/IEC 17025 could thus be directly transferred and adapted. The ISO/CASCO is responsible for the correct application of its standards and their integration into the overall context of international standardization.

The development of an international standard takes place in consensus with all involved experts, in correlation of the different projects within the working group and in interaction with the other working groups of the TC. Within the framework of international meetings, structured comments and coordination between the experts take place. The development cycle of the standard is shown schematically in Figure 4.

ISO 20387 has been available internationally since 2018. Based on the general requirements of ISO 20387, technical specifications and substandards (e.g. ISO 20388, 20389) will continuously supplement these. Figure 5 illustrates the structure of the family of standards around ISO 20387 [31]. The Technical Report on ISO 20387 prepared in parallel with ISO TC 276 is to be understood as a guide to implementing the requirements of ISO 20387. It also provides information on how the requirements can be integrated into an existing QMS. Finally, links to additional resources, including international and national standards and accreditation bodies, are included in the bibliography.

Proof of conformity with a standard

Conformity with an industry-specific standard can prove a defined purpose and performance (competence). The applied QMS principles enable the demonstration of an efficient use of resources, optimize risk management and increase user satisfaction and safety. The applicable EU directives and regulations allow IVD manufacturers to use harmonized standards as evidence. During an audit or review of the technical documentation, it should be possible to decide as clearly as possible whether relevant requirements have been met. Standards contain such specific criteria. Standards represent the minimum consensus, i.e. a level that a professionally acting company should not fall

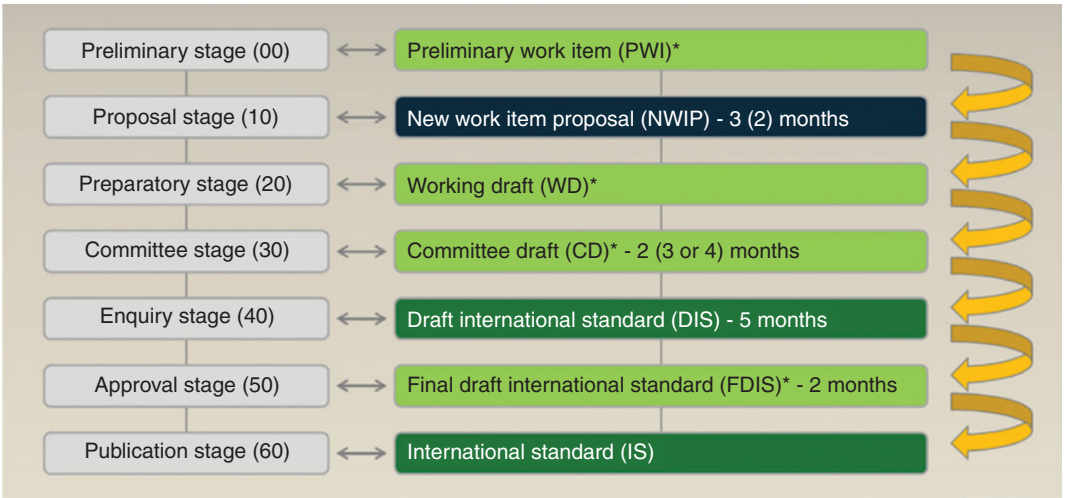

Figure 4: Development cycle of the standard [34].

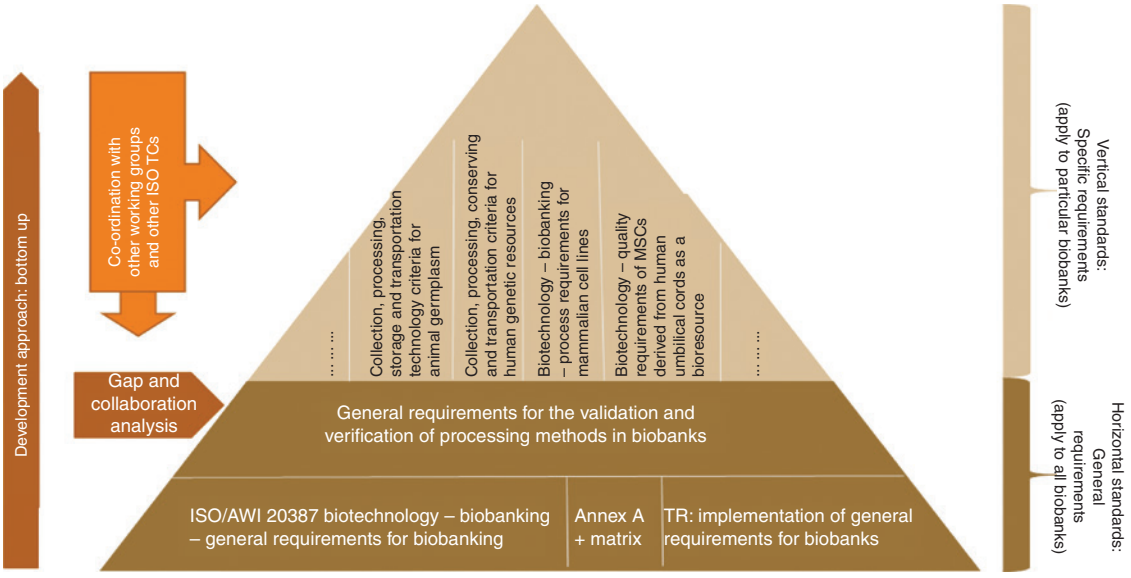

Figure 5: Road-map of the biostandard [31].

below. For manufacturers, the following applies in principle: If a CA procedure (e.g. according to Annex II of the MDR or Annex IX of the MDR) requires a QMS, manufacturers must have this QMS certified by a notified body. Certification of manufacturers to individual standards is not required, but it can be expedient for manufacturers to recruit cooperation partners with appropriate proof of competence (https://www.johner-institut.de/blog/regulatory-affairs). The qualification of study laboratories is already common practice [35, 36]. Some institutes have their own areas for carrying out laboratory testing within the framework of clinical studies and are accredited by DAkkS according to DIN EN ISO/IEC 17025 and are recognized by the Central Office of the Länder for Health Protection with regard to Medicinal Products and Medical Devices under the terms of the Council Directive 98/79/EC and EN ISO/IEC 17025. Proof of accreditation and an established quality assurance programme by means of corresponding interlaboratory comparison certificates is obligatory today. In this context, multi-center projects at the national and international levels pose a challenge [2]. At this point, a qualification of the partners through comparable proofs of competence facilitates the recruitment of study partners for the sponsors.

Possible CA practices associated with each of the aforementioned guiding principles are manifold. Basically, a distinction can be made between:

Accreditation

Confirmation by a third party that formally states that a CAB has the competence to carry out certain CA tasks (ISO 17000) [37].

Certification

Procedure by which a third party confirms in writing that a product, process, system or person conforms to specified requirements (ISO 17000) [37].

ISO 20387 and accreditation

From 2015, accreditation bodies were also approached for active cooperation in TC 276. In addition to the German Accreditation Body GmbH (DAkkS), representatives of the Japanese Accreditation Body (JAL) also participated. In 2017, representatives of the GBA founded a working group with DAkkS, which, if possible using existing structures in the field of biobanks, should enable an accreditation soon after the publication of the standard in Germany. Parallel to the standardization procedure, the accreditation requirements are prepared here. To this end, the following challenges, among others, must be mastered

- Definition of the scope
- Creation of an accreditation program
- Development of a concept for the long-term cooperation of the accreditation body with the "interested parties and stakeholders"
- Setting up and training of a pool of assessors

After ISO 20387 was published in August 2018, ILAC (international organization for accreditation bodies operating in accordance with ISO/IEC 17011) resolved in ILAC Resolution GA 22.19 that the standard applicable to biobanks for the purposes of accreditation will be ISO 20387 Biobanking – General requirements for biobanking, to be used as a standalone standard.

In November 2018, European Accreditation (EA) approved this resolution as applicable to EA and its members (https://ilac.org/publications-and-resources/ga-resolutions, https://european-accreditation.org/wp-content/uploads/2018/11/AI_15-EAGA1811-36-RESOLUTIONS_42-GA-22Nov2018-FINAL.pdf).

As accreditation according to ISO 20387 was demanded by German biobanks, the German national accreditation body (DAkkS) developed an accreditation program based on this standard and launched it in September 2019. Other accreditation bodies also started to work with ISO 20387, e.g. A2LA granted the first accreditation based on this standard in spring 2019 in the US and the national accreditation body of UK (UKAS) also started a project to develop an accreditation program for biobanks in the UK.

Parallel to the development of accreditation programs in different countries, the ISO standard was forwarded to CEN/CENELEC to transform it to an EN standard that can be implemented as harmonized EN standard within the scope of Regulation (EC) No. 765/2008 by the EU.

Conformity assessment and scope

In the context of an accreditation, the scope determines a clearly defined description of the specific CA activities for which a specific biobank holds accreditation. According to ISO 20387, there are some activities a biobank has to fulfil to meet the requirements of the standard and others that optionally could be fulfilled by the biobank and confirmed by an accreditation body. The description of the scope in a specific biobank includes the biobanking activities as well as biological material/associated data and procedures used for the activity. Hence, this scope of accreditation is different from one biobank to the other.

The description of the scope is a complex challenge. The published scope should give a clear picture of the competence of a biobank in a way that is understandable for the customers of the biobank and comparable between different biobanks if they perform comparable activities. The scope should refer to the relevant processes and applied methods. These methods refer to the processing of the biological material and associated data as well as to the measurement and testing methods in place for quality control and qualifying tests relating to the fitness for the intended purpose.

Figures 6 and 7 show the selection process prior to the accreditation process, in which the area of application of ISO 20387, for which the biobank seeks proof of conformity, will be defined. Each process within a certain scope shall be proved by a reproducible and quantifiable method.

The accreditation certificates disclose the scope, the biological resource(s) and associated data, the methods and metrological parameters. Working with the standard is voluntary. Biobanks are able to use it to check their processes and can try to fulfill parts or all of the standard requirements. Biobanks that have decided to fully comply

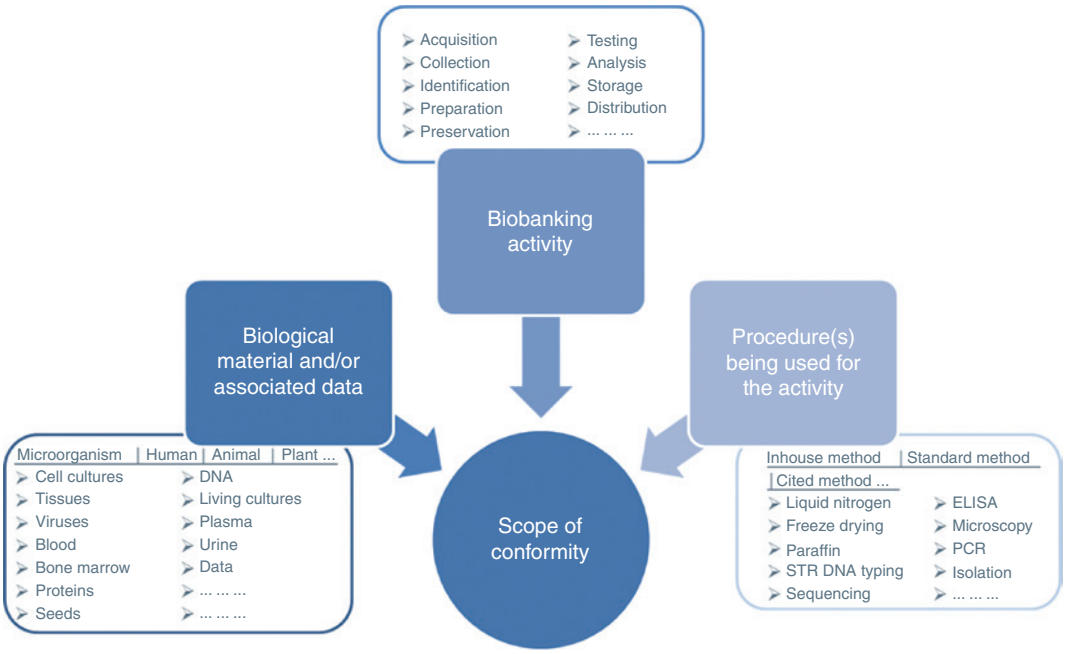

Figure 6: Scope of application of ISO 20387 in the context of accreditation.
Source: Dunja Martin, 2019.

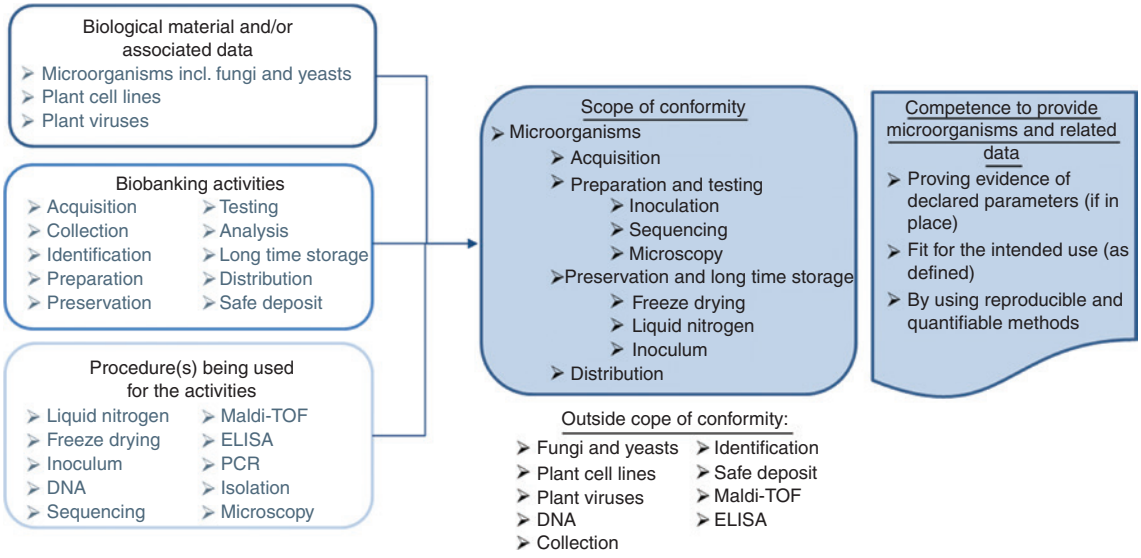

Figure 7: Area of application of ISO 20387.
Source: Dunja Martin, 2019.

with normative requirements could apply for accreditation as external confirmation of their competence. Through accreditation, a biobank can present itself to the market in such a way that it verifiably (confirmed by an independent body) is competent to meet the requirements of ISO 20387. The following principles apply: The biobank must fully meet the requirements of the standard (if applicable) within the framework of accreditation. The accreditation body confirms that the biobank meets the requirements of ISO 20387 for clearly defined areas (confirmation of competence for defined accreditation scope). Many biobanks have already set up a QMS in the past. Some are accredited for parts of their activities, e.g. as testing laboratories according to DIN EN ISO/IEC 17025, as inspection bodies

according to DIN EN ISO/IEC 17020 or as manufacturers of reference materials according to DIN EN ISO 17034. Others are certified, e.g. according to DIN EN ISO 9001. In addition, there are biobanks which are part of a larger organizational unit which is accredited as a medical laboratory according to DIN EN ISO 15189. ISO now ensures that CA standards that contain requirements for a QMS and can be used within the framework of accreditation are structured in a comparable way. Through the use of so-called "Common Elements", the requirements for the QMS are now very similar and comparable. For biobanks that have already established and introduced a QMS (as described earlier), this means that the QMS will largely meet the requirements of the new standard. Slight adjustments in detail may be necessary. However, this will be possible with little effort. Overall, we consider the possibility of a globally comparable standardization of the activities of biobanks as an important step toward the provision of high-quality and well-characterized biological materials. These are needed to enable a significant cost reduction through less faulty studies and research results based on poorly characterized biological materials. The chosen path enables the individual biobanks, based on their needs, to decide for themselves in which form they want to implement the requirements of the standard and present this to the market. The spectrum ranges from no implementation to partial or complete implementation with corresponding self-declaration to independent confirmation of competent implementation within the framework of accreditation.

Summary

Overall, standardizing the activities of biobanks is an important step toward providing high-quality and well-characterized biological materials to support modern biomedical research. Biobanks are important cooperation partners for the various players in the field of biotechnology, both at the academic and industrial levels. They must align their activities to the needs of users. The reduction of erroneous or non-reproducible study results on the basis of insufficiently characterized biological materials and the improvement of the interoperability of individual biobanks justifies the extensive effort involved in implementing the standardization requirements. Implementation aids published parallel to the standards support the implementation of the requirements. Umbrella organizations of biobank communities such as International Society for Biological and Environmental Repositories, European, Middle Eastern, and African Society for Biopreservation and Biobanking (ESBB), TMF and GBA also offer different support instruments to jointly achieve interoperability and sustainability. The European Commission is increasingly integrating standardization requirements into its tender texts. The use of standardized procedures and CA is evidence of competence and is the key to participation in large networks. Standards thus ensure the sustainability of the sample collections and justify public funding. Active participation in the creation of standards in the field of biotechnology and bioresources means being able to shape and influence the content of standards. The experts are integrated into a network and thus generate a knowledge advantage. Usage strategies can be designed or pursued here, as the standardization committees are not only composed of the future users of the standards and regulations, but also of potential customers. Through their cooperation, the GBA experts, for example, have the opportunity to acquaint other biobank communities and potential users with their activities and gain additional insights into current developments in Europe and worldwide, as standardization work today takes place under international signs. This results in sustainable future models. ISO's chosen path of elevating ISO 20387 to a CA standard enables the individual biobanks to decide for themselves how they want to implement the requirements of the standard and present them to the market. The spectrum ranges from non-implementation through partial or full implementation with corresponding self-declaration to independent confirmation of competent implementation within the framework of accreditation. Due to the increased requirements of biomedical research, accredited biobanks in particular will have a competitive advantage in the future.

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