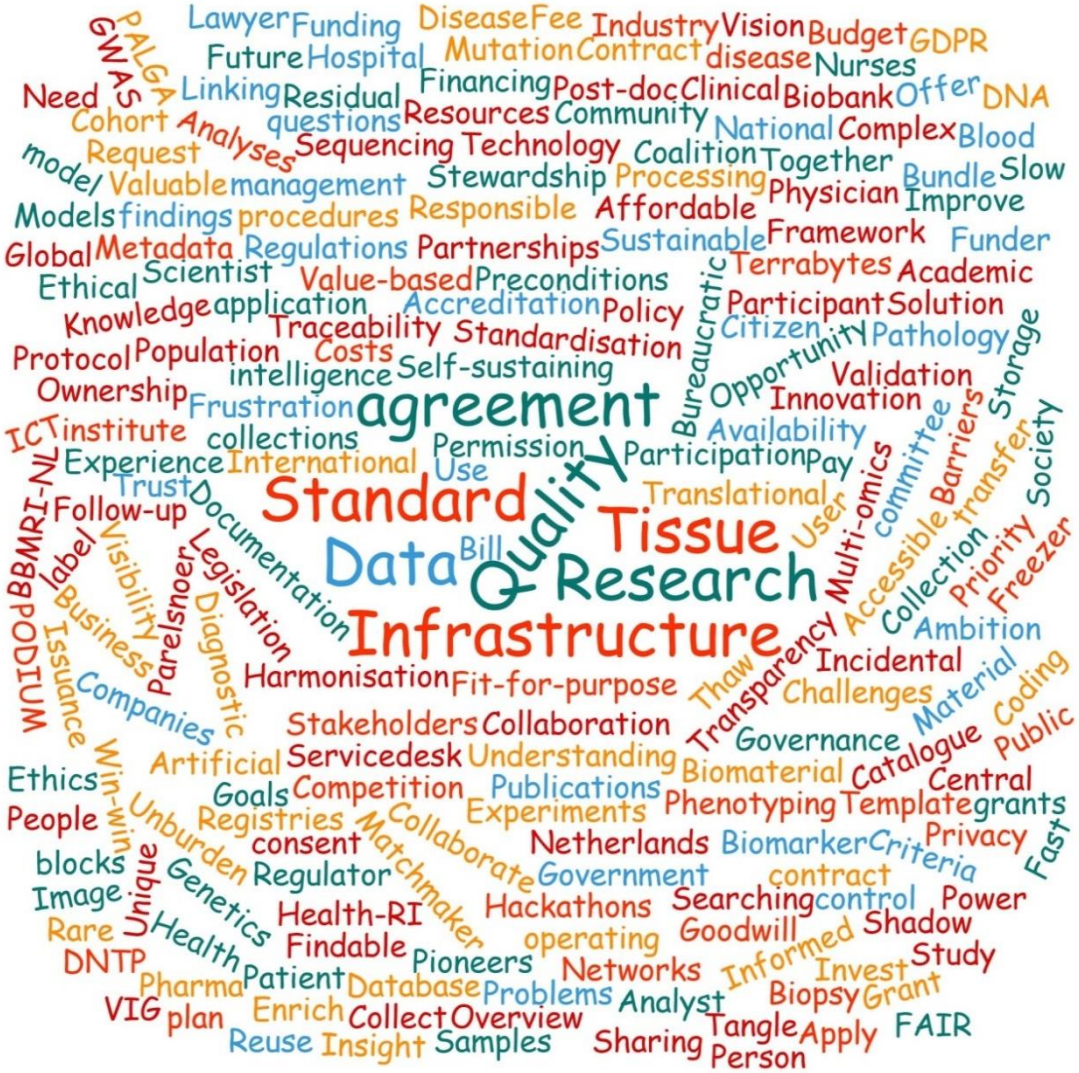
Creating an Environment for Sustainable Biobanking in the Netherlands

Perspectives and Challenges of Dutch Biobank Users



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Management summary

Introduction

Biobanks enable the collection, management, and use of samples and data for medical research. By providing the necessary sample size, data depth, and statistical power they are essential for answering contemporary biomedical research questions. In addition, biobanks directly enable translational research, bringing new knowledge, treatments, and health innovations within closer reach.

To deliver tangible results biobanks need to operate for prolonged periods of time, or in other words, in a sustainable manner. To achieve sustainability, biobanks must balance their operational, social, and financial dimensions. However, sustainability is a challenge for many biobanks. An unsustainable biobank is a waste of samples, data, time, and, often public, funds. As such, biobank sustainability is a pressing issue for both individual biobanks, national and international policymakers and funders, patients, researchers, and other involved stakeholders.

Individual biobanks are responsible for their own sustainability. However, they are also dependent on their surrounding macro-environment, which contains factors that either promote or impede sustainability. To maximise biobank impact we need to create an environment that contains the financial, legislative, and policy prerequisites beneficial to sustainable biobanking. It is the responsibility of all involved stakeholders to make efficient and effective use of available resources and thus enable an environment in which biobanks can be sustainable. To obtain a clearer picture of existing challenges we initiated a dialogue with various Dutch biobank users, to gather their experiences, needs, and challenges.

Methods

We organised four focus groups, three with users from academia; organised at the Netherlands Cancer Institute, the Radboud University Medical Center, and the University Medical Center Groningen; and one with users from private industry, in collaboration with the Dutch Association Innovative Medicines. A total of 24 participants enrolled, including PhD/MD-PhD candidates, post-docs, senior researchers, professors, team leaders, and higher-level managers.

Main results

Analysis of the focus group recordings resulted in the list of topics:

- Quality: Biobank users stated that sample and data quality is essential for research, health care impact, and long-term usability. However, numerous quality problems persist, mostly regarding missing or incomplete metadata. Private industry places high demands on quality, especially in the area of documentation, as they have to comply with strict regulatory standards. For biobanks seeking public-private partnerships, collaboration should occur before collection starts, to prevent an irreparable mismatch. All users indicated that a higher level of interoperability between samples and different data sources should be achieved to increase biobank value.
- Accessibility: The current policy is to make biobanks FAIR (Findable, Accessible, Interoperable, and Reusable), however, all focus groups mentioned problems with FAIRness. Both users from academia and industry indicated difficulties in finding samples and data for their research. In addition, all focus groups encountered problems with accessibility and collaboration.
- Ethical, legal, and societal issues: Users state they need additional support on matters such as privacy, data protection, and data sharing, as current legislation is confusing. In addition, there is significant variability between institutes, and in policies related to informed consent, unsolicited findings, standardised agreements, contracting, and medical ethical reviewing; resulting in lengthy procedures. Users urge for more harmonisation on all these topics.

- Financing: Users from academia indicate that research funding in the Netherlands is predominantly focused on funding project staff. Funders are also willing to pay for the costs of collecting samples and data. However, academic users state that funders should encourage and facilitate the use of samples and data from existing biobanks, for example by shifting budget for initiating *de novo* collections towards reuse of current collections.
- A biobank's role as supporting infrastructure: In general, users from academia indicated that biobank-related tasks such as data management, data sharing, and legal issues were often transferred to them as users, while they expected such support to be provided by the individual biobanks themselves or by the local or national biobank facilities.
- Industry perspective on academic biobanks: The pharmaceutical industry looks for biobanks with clinical data linked to samples. Genomic sequencing data for mutation analyses, target identification, and new biomarkers, is also high on the list. In all cases, sufficient critical mass is important. Public-private biobank collaborations remain challenging due to difficulties in finding the right samples and data, lengthy contracting procedures and differences in quality standards and requirements between academia and private industry.

Discussion

All users considered biobanks to be crucial infrastructures for translational research. However, they also pointed out that further improvements to quality, accessibility, harmonisation and funding are necessary to increase their potential use and impact.

Based on the focus group responses we identified four additional topics of discussion: 1) Data is the way forward in biobanking; 2) Users look for some sort of quality mark to confirm which biobanks to collaborate with; hereby adopting a broader concept of quality than just the collected samples and data; 3) the Netherlands must continue to promote biobanking collaboration to counteract national fragmentation; and 4) The expectations of users regarding BBMRI-NL do not correspond to reality. Therefore, BBMRI-NL should communicate more clearly towards all stakeholders what their mission and vision is and what goals they are pursuing in order to prevent a mismatch between expectations and reality.

Next steps

Improving the sustainability of biobanks requires effort from all involved stakeholders. The results from these focus groups will be combined with the input gathered from biobanks themselves (van der Stijl, Scheerder, and Eijdems 2018) to create stakeholder-specific recommendations. These recommendations will serve as a starting point for discussions with stakeholders; such as funders, patients, policymakers, and the general public; to define suitable overarching prerequisites for sustainable biobanking. Only through joint action can we create a macro-environment that enables and promotes sustainable biobanking for the benefit of medical research, health care, and the Dutch population.

1. Introduction

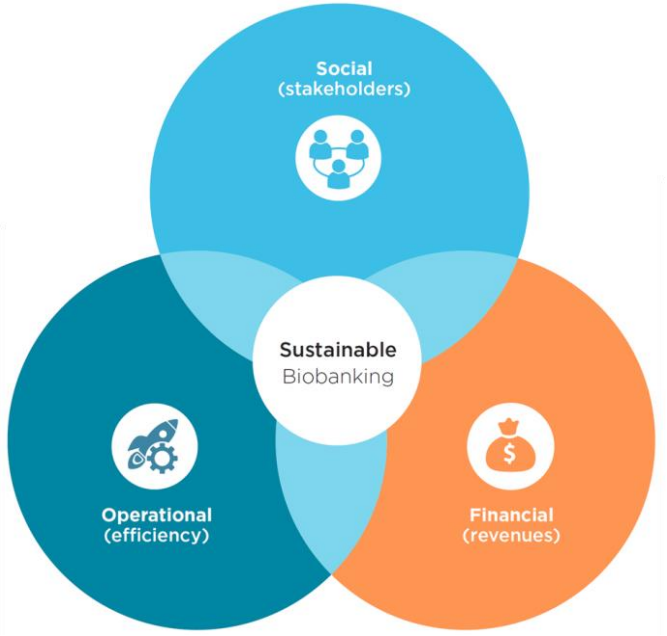
1.1. Sustainable biobanking: a theoretical framework

Biobanks[1] enable the collection, management, and use of samples and data for medical research. To deliver tangible results, biobanks (and similar health data infrastructures such as medical registries and imaging databases) need to operate for prolonged periods of time. Thus, biobanks need to be sustainable to deliver on their promise of health care innovation.

> *Sustainability is the capacity of a biobank to remain operative, effective, and competitive over its expected lifetime.*
> (OECD Global Science Forum 2017)

However, it is precisely sustainability that is considered a challenge (Cadigan et al. 2013, 1-7819-9-1; Watson et al. 2014, 60-68; Stephens and Dimond 2015, 417-436; Timmons and Vezyridis 2017, 1242-1257; van der Stijl et al. 2018; Rao et al. 2019, 129-138). Biobanks operate in a complex environment at the interplay of ethical, scientific and commercial values. They have to meet a range of expectations from both science and society and a growing demand for quality, FAIRness[2], transparency, and accountability. In addition, during their operation, biobanks are faced with technical, legal, and financial issues. As such, sustainable biobanking is a pressing issue for both individual biobanks and for national and international policymakers and research funders.

Figure 1. A framework for sustainable biobanking



The framework for sustainable biobanking consists of the overlapping financial, operational, and social dimensions. To become sustainable, biobanks need to balance these three dimensions in the context of their own individual situation. Figure adjusted from (Watson et al. 2014, 60-68).

[1] There are many forms of biobanks and accompanying definitions. This report adheres to the broad definition adopted by BBMRI-ERIC: *Biobanks are collections, repositories and distribution centres of all types of human biological samples, such as blood, tissues, cells or DNA and/or related data such as associated clinical and research data, as well as biomolecular resources, including model- and microorganisms that might contribute to the understanding of the physiology and diseases of humans* (European Commission 2016, Chapter 1, Article 1 (1)).

[2] FAIR stands for Findable, Accessible, Interoperable, and Reusable. For more information see: https://www.go-fair.org/fair-principles/ (Wilkinson et al. 2016, 160018).

Watson and colleagues have developed a holistic framework to better understand sustainable biobanking. Their framework consists of three overlapping dimensions – operational, social, and financial – encompassing all aspects that play a role in biobank sustainability (see figure 1). The operational dimension is about a biobank's efficiency, involving aspects related to a biobank's input, internal and output processes (e.g. sample collection and processing, organisational structure, standard operating procedures). The social dimension relates to the interaction and relationship with a biobank's stakeholders (e.g. donors, funders, users). The financial dimension is concerned with a biobank's available resources and how these resources are generated and used (e.g. funding, costs). To be sustainable, a biobank has to continuously balance these three dimensions to create value.

Individual biobanks are responsible for their own sustainability. However, they also depend on their surrounding macro-environment, which contains factors that either promote or impede their sustainability. Creating a macro-environment that contains the right financial, legislative, and policy prerequisites for sustainable biobanking will benefit medical research and, ultimately, health care. Finding and defining these prerequisites will require a collaborative effort from all stakeholders involved.

1.2. Project setup and goals

Globally our project aims to improve the sustainability of individual biobanks and the Dutch biobanking infrastructure as a whole by determining suitable overarching preconditions for sustainable biobanking. To get a clearer picture of the existing challenges and to search for possible and desired solutions we gathered input from both biobanks (van der Stijl et al. 2018) and their users[3]. For the latter, we organised four focus groups in spring 2019 with Dutch biobank users from academia and private industry; the findings of which are presented in this report. Our goal was to collect the experiences, needs, and challenges from the perspective of different Dutch biobank users.

By gathering input from both the supply (biobanks) and the demand (users) perspective we aim to identify those challenges that cannot be solved by individual biobanks, but instead should be resolved on national collaborative level. The findings are a starting point for broader discussions with additional stakeholders; funders, patients, policymakers, and the general public; on which overarching prerequisites are desirable and need to be defined to improve sustainability in the biobanking field.

1.3. Focus and scope

The report focuses on Dutch users of academic biobanks containing human samples and data for scientific research. However, the content of this report can also be useful for collections consisting exclusively of data (e.g. medical registries), for non-human sample and data collections, and for international biobanks.

1.4. Organisational context

Creating an Environment for Sustainable Biobanking in the Netherlands: Perspectives and Challenges of Dutch Biobank Users is a product of Biobanking and BioMolecular resources Research Infrastructure The Netherlands (BBMRI-NL) work package 6: Sustainable and Interactive Biobanking. It is part of a BBMRI-NL Series on Sustainable Biobanking. BBMRI-NL is an initiative of the eight Dutch university medical centres, other Dutch research centres and organisations, as well as the Parelsnoer Institute. BBMRI-NL is part of Health-RI, the overarching Dutch research infrastructure on

[3] A user is a person or party that makes use of the samples and/or data gathered by a biobank. Users can be researchers from universities, hospitals, or research institutes; the pharmaceutical industry; biotechnology companies; small- and medium enterprises; or government institutions. Users can either have access to their own biobank or use a biobank from a third party. There are also potential users; parties that might use a biobank in the future but have not done so for various reasons.

personalised medicine and health data. In addition, BBMRI-NL serves as the Dutch node of the European network of biobanks, united under BBMRI-ERIC.

2. Methods

2.1. Focus group setup and analysis[4]

To gather experiences, needs and challenges of Dutch biobank users[3] we organised four two-hour focus groups; two in March 2019 and two in May 2019, according to the focus group manual of Centraal Begeleidingsorgaan, a Dutch health care quality institute (Anonymous2004). We choose to organise focus groups as this method is useful to obtain both detailed and broad information on perceptions and opinions on a specific subject. In addition, focus groups can provide in-depth information due to discussions between participants and allow asking clarifying follow-up questions. Possible disadvantages are the potential of group conformity and potential selection bias due to the smaller sample size compared to, for example, a widely distributed survey. We are aware that the focus groups constitute only a part of the varied biobanking field. Still, the results gathered at multiple organisations provide valuable input to further improve the Dutch biobanking field.

Of the four focus groups, three included only academic users. These were organised at the Netherlands Cancer Institute, the Radboud University Medical Center, and the University Medical Center Groningen. The fourth focus group included only users, or potential users, from private industry; more specifically the Dutch departments of the pharmaceutical companies Amgen, AstraZeneca, Boehringer Ingelheim, Novartis, and Roche, and the Dutch industry association for contract research organisations ACRON. This fourth focus group was co-organised with the Dutch Association of Innovative Medicines (Vereniging Innovatieve Geneesmiddelen). See 2.2 for a description of the organising parties.

A total of 24 participants enrolled in the focus groups, constituting a 9 to 15 male/female ratio. At each academic focus group there was a non-participant representative from the organising party. The company focus group was joined by a non-participant from Health-RI. The academic participants included PhD/MD-PhD candidates, post-docs, senior researchers, research analysts, project managers, data managers, medical doctors, and professors. All academic participants had experience with requesting and using samples and data from Dutch biobanks (e.g. PALGA, AGORA, NESDA, Lifelines), and some with international biobanks (e.g. UK Biobank, Twin's UK). What stood out was that most academic participants stayed close to home, using biobanks in which they themselves or their department or institute were involved. The company focus group included higher level managers and team leaders. Only one of the companies had thus far been able to establish a successful collaboration with an academic biobank despite attempts by multiple of the participating organisations.

Participants for each focus group were approached by the local organising party. The aim was to select for a good gender, age, and function distribution. In the end, willingness and time to participate was often the deciding factor. Participants for the University Medical Center Groningen focus group were selected via the local biobanks and the research register; and approached by R. van der Stijl via email, telephone, or face-to-face. At the Radboud University Medical Center all researchers who had previously used samples and data from the Radboud Biobank and were still working at the institute were contacted by P. Manders via e-mail. Participants were those who were available on a specific date. Those who could not participate had a legitimate reason, e.g. they had to perform clinical tasks or were attending a conference. Participants from the Netherlands Cancer Institute focus group were broadly invited via email by A. Broeks from the pool of current Core Facility Molecular Pathology and Biobanking users. Participants for the Association of Innovative

[4] For the methods section we followed the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist as closely as possible (Tong, Sainsbury, and Craig 2007, 349-357).

Medicines focus group were approached via their working group Real Life Data. All focus group participants were informed via email beforehand about the goal and setup of the focus groups.

The focus groups were conducted in Dutch according to a predetermined questionnaire (see 7. Appendix for the questionnaires of the academic and private industry focus groups, in English and in Dutch). The questionnaire was reviewed before use, but not pilot tested. Clarifying or specifying questions were used by the facilitator in addition to the predetermined questionnaire. The first hour of each focus group focused on biobanking in general. During the second hour questions focused on the local situation of the organising party. For the company focus group the full two hours were spent on discussing academic biobanking in general.

All focus groups were facilitated by R. van der Stijl. He holds a master degree in Medical & Pharmaceutical Drug Innovation and in Science, Business & Policy, and works as a project manager for the UMCG Research BV. He has experience in facilitating workshops, round table discussions, meetings, and general assemblies. Together with Lisette Eijdems, he executes BBMRI-NL's sustainable biobanking project. As a temporary project officer, he has no direct stake in the outcome of this project. In addition, he has currently no role in the University Medical Center Groningen's biobanking activities.

Audio recordings were made of each focus group and were transcribed by the authors. P. Manders and R. van der Stijl both translated, independently from each other, the transcripts of all four focus groups into a list of topics and subsequently compared their results. This comparison resulted into a final list of topics that served as a basis for this report. Before publication, a draft of the report was sent to all focus group participants for corrections and comments.

2.2. Description of the participating organisations

Netherlands Cancer Institute (NKI) – Core Facility Molecular Pathology and Biobanking (CFMPB)

The NKI is a cancer research institute and part of the Antoni van Leeuwenhoek hospital, combining research and patient care. The NKI has multiple secondary use and de novo biobank collections, of which the use of samples is managed by the CFMPB. Tissue blocks constitute a large proportion of the available samples. For all NKI research projects, researchers need ethical approval from the institutional review board. Subsequently, the CFMPB handles sample logistics, generates derivative samples, performs all kinds of single and multiplex immunohistochemistry and molecular analysis, and stores scientific results. Currently the facility consists of 12 technical and administrative staff members, dedicated lab space and equipment (e.g. a histology/immunohistochemistry lab), and an in-house developed sample application and request tool.

Radboud University Medical Center (Radboudumc) – Radboud Biobank

The Radboudumc specialises in patient care, scientific research, teaching and training. Established in 2012, the Radboud Biobank serves as centralised biobanking infrastructure for disease-specific biobanks within the Radboudumc. The Radboud Biobank, with a team of 10 staff members, supports researchers throughout the entire organisational process of building and using a biobank by managing the biomaterials and the associated clinical data, providing long-term storage, and standardisation in the areas of ICT, legal-ethical aspects, biobanking, communication and distribution. The goal is to support researchers to achieve ground-breaking innovations in translational research via standardised collection, storage, and management of biomaterials together with detailed clinical data (Manders et al. 2018, 2).

University Medical Center Groningen (UMCG)

The UMCG is the only university medical centre in the North of the Netherlands, and one of the largest in the country. The UMCG brings together patient care, with a focus on complex care, rare diseases, and comorbidities, education and research. The overarching research theme is healthy and active ageing. The UMCG houses multiple clinical and population biobanks. Coordination lies with the principal investigator of each individual biobank. Samples are stored in a centralised freezer facility and biobanks must follow the UMCG Biobank Regulations. Expertise on different biobanking aspects,

such as specific sample analysis, data storage, research design, bioinformatics, bio-imaging, laboratory processes, legal and regulatory affairs, quality, and privacy, is spread over individual UMCG departments.

Association of Innovative Medicines (Vereniging Innovatieve Geneesmiddelen) – Working Group Real Life Data

The Association of Innovative Medicines is the Dutch industry association for pharmaceutical companies focused on innovative biotechnological medicines. The association consists of 43 member companies. Its main task is to demonstrate the sector's importance to health care, influence decision-making, and provide information and services for its members. The association has 24 employees, including experts in the fields of health care economics, pharmaceutical affairs, innovation, biotechnology, medical-scientific issues, legal affairs, and communication. The employees of member companies are actively involved in policy-development through theme-based working groups.

2.3. Discussion on focus group execution

Several comments can be made about the execution of the focus group methodology. Firstly, the topic of biobanking is diverse and therefore open to interpretation by the participants. Despite introducing this issue at the start of each focus group, the viewpoint of the participants on biobanking and their role as user was influenced by how biobanking was organised within their local hosting institute. However, as the goal was to gather diverse viewpoints, this only helped to approach biobanking from multiple perspectives.

Secondly, we used the same questionnaires for all academic focus groups (see 7.1 and 7.2 for academic focus group questionnaires, in English and Dutch). However, for the company focus group the questionnaire was adjusted to better reflect their different position as user group, asking about their perspective of academic biobanks (see 7.3 and 7.4. for the industry focus group questionnaire, in English and Dutch). There was still considerable overlap to allow for a comparison of results. During the focus groups the order of questions was adjusted to better fit the on-going discussion and sometimes questions were skipped due to time constraints.

Finally, the focus groups and questionnaires were conducted in Dutch, while the report is in English. We cannot exclude a loss of information due to this translation. This is also valid for the quotes shown in the report, which are paraphrased as closely as possible to the original Dutch text. In some quotes we added additional wording between [brackets] to set the right context.

3. Results

3.1. Why do we need biobanks?

"Consequences for the patient [of a world without biobanks]*: less research questions answered, less treatment options, lower quality of life."* – USER FROM ACADEMIA

The focus group participants indicated that biobanks are necessary to achieve the required sample size and statistical power to perform contemporary scientific research. This is especially true when studying rare diseases, but also true for genomics, proteomics, and metabolomics studies. Without biobanks to collect and pool sufficient, sometimes rare, biomaterials and associated data, many research questions can no longer be answered. A loss of biobanks will result in a reduction in research quality and validation. The participants also indicated that biobanks are important enablers of translational research. And a lack of translational research will negatively impact patient care in the long term.

"If you want to be competitive internationally you will get into serious trouble without biobanks."
– USER FROM ACADEMIA

Besides the consequences for patients, a lack of biobanks will also hurt the Dutch scientific position. According to the focus group participants, a large amount of biomedical scientific output is based on biobanks and biobank-related research. Furthermore, they state that contemporary high impact research requires more and deeper data on large numbers of participants, something that can only be accomplished through organised collection by biobanks and similar infrastructures. A loss of biobanks will thus lower the number and quality of publications, negatively affecting the standing of Dutch researchers and their ability to attract external research funding and top talent.

The experience of academic users is that, despite the voiced need for biobanks, academic researchers still collect samples and data for their own use, disregarding existing biobanks. The users believe this occurs for a number of reasons, for example if the samples and data a researcher needs are not available, either due to access restrictions or because no one has collected them yet. In addition, some researchers tend to mistrust samples and data collected by others, preferring to collect and "control" everything themselves, despite the inefficiency and potential quality issues. In reality, this leads to continued duplication of collections, underpowered "convenience" collections with local biases, and increased strain on the research system trying to sustain all these collections (Rush et al. 2019, 219-229). To prevent the unnecessary collection of samples and data by researchers themselves, biobanks need to make sure they are findable, accessible, and fit-for-purpose for contemporary research.

3.2. Quality

"How on earth are things done?" – USER FROM ACADEMIA

All focus groups stated that samples and data quality is essential. However, they also indicate difficulties in determining the actual quality of collected samples and data. Standard operating procedures, uniform collection and storage conditions, appropriate metadata on sample and data origin, processing and usage history, and proper data management and control are considered indicators of quality and major requirements for biobanking and biobank-related research. High quality improves the long-term usability of collections. However, users state they still encounter numerous quality problems. Appropriate metadata, including historical processing and usage data, are often lacking. Researchers want to know what already has been investigated in a certain sample to prevent repetition of analysis. In addition, researchers spend a lot of time managing, checking, and correcting data, while they indicate that this responsibility should lie with the biobanks themselves.

"We have a 16-page protocol for collecting those samples. Academic biobanks will not be able to meet those requirements." – USER FROM PRIVATE INDUSTRY

Although both academia and private industry emphasize the importance of quality they use a different quality standard to determine if samples and data are fit-for-purpose. This is because the commercial environment is fundamentally different from the academic research environment. Private industry needs to meet the strict standards set by regulators. Therefore, they place high demands on samples and data quality, requiring strict quality assurance, collection protocols, and extensive documentation before being able to use the collected samples and data in their research and product development. The documentation performed by academic biobanks is often insufficient to meet the standards set by regulators, which makes the collection unusable for the pharmaceutical industry. The users from private industry suggested developing a list of preconditions that academic biobanks should meet if they want their samples and data to be fit for collaboration with private industry. But most of all, to prevent a mismatch, companies should collaborate at an early stage,

before collection starts, to contribute with their knowledge on protocoled reporting and documentation.

"If I had told my global chief medical officer that we had found a [Dutch] academic biobank with [samples] linked [to] clinical data, he would have flown in immediately." – USER FROM PRIVATE INDUSTRY

In order to increase interest in and the value of sample and data collections, all users indicated that a higher level of linkage between samples and different data types and data sources should be achieved. It is unlikely that we can reach the level of linkage demonstrated in Estonia and the Scandinavian countries that use the individual social security number. However, there are possibilities for improvement considering the Netherlands has several high-quality and nationwide medical and socioeconomic registries, such as the national cancer registry, registry of death certificates, and the Dutch pathology archives. Biobanks with samples linked to clinical and phenotypic data are considered invaluable, especially if this data includes sequencing data and follow-up information. Data on a participant's disease course and outcomes can be obtained either by follow-up visits or by linkage to already existing national health registration systems. Unfortunately, biobanks are often not linked to such available databases, mostly due to technical, methodological and/or legal limitations of data linking. Even though the Netherlands is not yet at the level of some other countries, much has been achieved in recent years, linking individual Dutch biobanks to large data registries.

3.3. Accessibility

"Everyone says FAIR, but nobody does FAIR." – USER FROM ACADEMIA

Creating a sustainable biobank means developing a secure environment in which other researchers can access the samples and the data; taking into account the privacy of the participants and other relevant safeguards. The samples and data in a biobank must be Findable, Accessible, Interoperable, and Reusable (FAIR)(Wilkinson et al. 2016, 160018). However, all focus groups mentioned problems with FAIRness. Both users from academia and private industry stated that they had trouble finding the samples and data they needed for their research; despite the BBMRI-NL catalogue listing many available biobanks and collections. However, even with such a catalogue, users indicated collections were missing or had incomplete information, limited metadata, or unclear or limited access conditions; all major obstacles for finding and acquiring the necessary samples and data.

All focus groups encountered problems with accessibility. Even when samples and data were available, some biobanks were just not open to sharing or collaborating. This applies to both collections that are included in the BBMRI-NL catalogue and collections that have not yet been included. There can be various reasons for this lack of sharing. There could be too many sample and data requests and a shortage of manpower or funding to process them. Or there could be legal barriers, for example in the informed consent. However, sometimes the will to share is simply lacking. Even though a patient has given written consent that the material may be used for future research, the collecting researcher (principal investigator) sometimes tries to maintain control and keep the samples and data for his or her own use. This behaviour is in some ways understandable as it takes the collecting researcher tremendous time and effort to include all participants and collect the samples and data. Furthermore, as competition between researchers is high, biobanks wish to conduct the research themselves. In practice, this restricts the use of valuable, publicly-funded collections. Although the FAIR principles and the sharing of samples and data has gained wide theoretical support, for some parties there seems to be greater hesitancy in practice.

3.4. Ethical, legal, and societal issues (ELSI)

"[Medical ethical review] takes a lot of time, and each institute has its own way of working."

– USER FROM ACADEMIA

Users stated a need for support on matters such as privacy, data protection, and data sharing. What is the policy for international sharing of data and samples? How should a researcher deal with unsolicited findings? Both the users from academia and from private industry stated that the current legislation is unclear; it is a maze and open for interpretation. As a result, users experience a significant variability between institutes in terms of informed consent procedures and procedures related to unsolicited findings. Furthermore, each institute has developed its own material and data transfer agreements (MTA/DTA). Harmonisation into a standard national MTA/DTA would simplify sample and data sharing. The Netherlands Federation of University Medical Centres is currently in the process of finishing a national template for a MTA/DTA.

There is also no consensus in the field of medical ethical reviewing. Local medical ethical review committees have their own procedures and policies, and are often unwilling to accept the outcomes of reviews done by other medical ethical committees. The result is that researchers have to perform a different ethical review at each institute, considerably slowing the sample and data application process or the initiation of new biobanks. So far, projects trying to align medical ethical reviewing of biobanks and biobank-related research within one standard Dutch policy framework were unsuccessful.

"Especially the academic centres are slowest with setting contracts. Community hospitals are much easier and faster." – USER FROM PRIVATE INDUSTRY

The users from private industry suggested drafting one model agreement that sets the standard for public-private biobank collaborations in the Netherlands. To get sufficient mass in samples and data, private industry often has to collaborate with multiple medical centres, each with its own legal department. Subsequently, negotiations must be conducted with each separate organisation on intellectual property, ownership, publishing, etc. And each organisation has different opinions, policies, and priorities on these subjects. The resulting slow progress, which the companies themselves also admit contributing to, ensures that many projects fail before they have even started. A model agreement would provide a starting point for negotiations and make clear to international parties under what conditions Dutch biobanks are willing to collaborate. Parties could always decide to deviate from such a model, accepting the consequence of slower progress. Such a public-private partnership model agreement has recently been drawn up for clinical trial studies (i.e. clinical trial agreement) by the Dutch Clinical Research Foundation, the Association of Innovative Medicines, and the Netherlands Federation of University Medical Centres, amongst others. Perhaps these and similar parties can use their experience to also draft a model agreement for public-private collaboration with Dutch biobanks.

3.5. Financing

"A biobank is just a library, and a library is never self-sustaining." – USER FROM ACADEMIA

In general, all academic users were willing to pay for the use of samples and data as long as the costs made by the biobank are transparent. Users want to pay for actual costs, i.e. what a biobank spends on processing, storage, maintenance, and transport of data and samples. Some users suggested that a price could be drawn up based on a general guideline. The shared opinion of all focus groups is that biobanks should not make a profit.

Research funding in the Netherlands is mostly focused on funding project staff. In addition, funders also fund the costs of collecting samples and data. However, users from academia experience limited availability of funding for requesting and analysing samples and data from existing biobanks, leaving researchers unable to pay a biobank's issuance costs. The academic users stated that a disproportionate amount of money is still being invested in setting up new biobanks, while

funding for maintaining and using existing biobank infrastructures is limited. Academic users indicated that funders should direct more funds towards the use of samples and data from existing biobanks, at the expense of the budget for initiating new collections. This would also enable a revenue stream from users towards biobanks, contributing to their sustainability.

"We are not only going to offer financial support, we want to contribute with our knowledge and participate in the planning and decision making [of a biobank]." – USER FROM PRIVATE INDUSTRY

Users from private industry expect biobanks to ultimately be self-sustainable. Private industry no longer wants to act purely as a cash machine to initiate and keep a biobank running. Instead they want to pay for the use of samples and data or initiate contract research agreements, where academic researchers answer the companies' research questions via a biobank's samples and data. The industry participants indicated that they are looking for partnerships and creating win-win relationships. This largely corresponds to the results from a recent German Biobank Alliance workshop on the cooperation between academic biobanks and pharmaceutical and diagnostics companies, where both sides stated that public-private research collaborations should be mutually beneficial (Baber et al. 2019, 372-374). In such collaborations, private industry is looking to contribute with their knowledge, expertise, and international network. In addition, they sometimes invest directly in the underlying infrastructure to enable a biobank to collect samples and data according to industry standards. The focus group from private industry indicated setting up public-private partnerships requires a long-term approach; something that can be difficult to reconcile with the often short-term focus of companies. In such public-private partnerships, the involvement of key opinion leaders and recognised centres of expertise with international visibility is important for private industry.

3.6. A biobank's role as an infrastructure supporting research

"It should be about the needs of researchers, not about the needs of the biobank." – USER FROM ACADEMIA

All users considered biobanks to be crucial infrastructures for translational research. However, the academic users also pointed out a need for more support for researchers that use biobanks. They indicated that tasks which they considered should be performed by other parties end up on their plate, for example on data management, data sharing, and legal issues. Some of the participants from academia stated feeling like involuntary guinea pigs, being the first to go through an issuance process and having to solve each obstacle by themselves. As most researchers lack the necessary expertise, such issues are considered to be a major source of frustration, a distraction from their main research tasks and a risk for failure.

The focus group participants from academia stated that additional support should be provided by the biobanks themselves or by national or local[5] biobank facilities, depending on the subject. Such support hubs would allow researchers a place to turn to instead of having to look for answers themselves. The focus groups indicated that local biobank facilities should focus on organisational and operational hands-on support, allowing researchers to focus on their research.

3.7. The industry perspective on academic biobanks

"So much data has been generated, but it is somewhere on a shelf, and it is still there. We could get a lot more out of that [data]." – USER FROM PRIVATE INDUSTRY

[5] The term local biobank facility refers to a centralised biobank infrastructure present within an individual institute, supporting multiple sample and data collections (e.g. Radboud Biobank).

The users from private industry state that biobanking and biobank-related research is mostly a matter for the global offices of pharmaceutical companies. The Dutch national company divisions are more focused on medical data registries. So what is the pharmaceutical industry looking for? The users from private industry indicate that next to brilliant research ideas, interest goes primarily to clinical data linked to samples to create well-phenotyped participants. The samples are sometimes even of secondary importance to the data. Genomic sequencing data for mutation analyses, target identification and new biomarkers, is high on the list. In addition, industry uses biobanks to stratify patients for clinical trials and to gather market information (e.g. how often does mutation X occur in the population?). In all cases, sufficient critical mass is important. One dataset from one medical centre is often insufficient for the industry. Sometimes the reverse happens and academic researchers approach industry for samples and data collected in the context of a specific clinical trial. The participants from private industry state that if they ask academic biobanks to be more visible and accessible, they themselves also have to open up more for academic researchers; all this within the legal and informed consent boundaries.

"In the past, [academia considered] the pharmaceutical industry scary. That is starting to shift here and there. Not everywhere [though]" – USER FROM PRIVATE INDUSTRY

The focus group participants from private industry pointed out that in the Netherlands, collaboration between companies and academic biobanks remains difficult. The participants could name just a single successful collaboration. Apart from not being able to find the right samples, they believe these difficulties originate from living in separated worlds. Academic researchers need to publish and are judged by their peers, while pharmaceutical companies need to bring products to the market and are judged by regulators according to strict standards. Private industry indicated they would benefit from a national biobanking matchmaker. Such a matchmaker would connect samples and data at academic institutions with research questions from private industry, and vice versa; similar to the role the Association of Innovative Medicines currently has for medical registries.

Industry users indicated that academic researchers can be fearful of collaborating with the industry, although this attitude is beginning to shift. Academic researchers and biobanks may benefit from public-private collaborations through joint publications, enhanced reputation and visibility, additional funding, and exchange of knowledge (Baber et al. 2019, 372-374). Such collaborations harbour considerable potential for the development of new therapeutics and diagnostics, and should be possible under the right conditions, taking into account ethical and legal safeguards and transparency towards donors and other stakeholders.

4. Discussion

The aim of this project was to gather the experiences, needs, and challenges from different Dutch users of samples and data from biobanks. Their perspectives will serve as input to improve the sustainability of individual biobanks and the Dutch sample and data infrastructure as a whole. The focus groups showed that, overall, users from academia and private industry underline the value of biobanks for research and society. Based on the focus group results, as described in the previous chapter, we detected four major topics that warrant additional discussion.

4.1. Data, data, data

In 2018, a group of experts from the International Society for Biological and Environmental Repositories (ISBER) stated that biobanking is not only the collection of samples but also of associated clinical data, allowing the meaningful study of the collected samples (Kozlakidis, Lewandowski, and Betsou 2018). It also emerged from the different focus groups that data is crucial. To answer contemporary scientific questions more and deeper data is needed. At the moment, much data has already been collected, but funds to enrich and analyse these existing datasets are

apparently limited. In addition, researchers often have doubts about the data quality, in part due to inadequate metadata. Further uncertainty amongst biobanks and researchers on data sharing and privacy issues was created by the introduction of the General Data Protection Regulation in 2018.

Despite these difficulties, it is clear that data is the way forward for biobanking. The use of real world data[6] through linkage with different data sources can enrich the data already gathered by biobanks. The development of Personal Health Environments[7] could add another dimension as citizens will be able to give dynamic consent for the use of their data and even contribute to collections via self-measurements (Eijdems, Boeckhout, and Zielhuis 2018). In addition, artificial intelligence and machine learning are creating new opportunities for researchers to explore their data and discover new insights on disease mechanisms and therapy outcomes. To get the most out of their data, life science researchers should collaborate with computer science or IT companies, as they bring in a fresh perspective and new knowledge. In addition, private industry has in-house artificial intelligence teams that are actively looking for research collaborations.

4.2. A Quality Mark to indicate biobank quality

Both the academic and industrial users indicated having difficulties in determining the actual value and quality of individual collections. Users are looking for confirmation on which biobanks they should trust and collaborate with and which samples and data to use. This goes beyond the physical quality of the collection and the applied quality standards, although these are definitely part of the equation. Users mention additional topics such as accessibility, FAIRness, transparency, governance, and collaborative options. Furthermore, one could add patient or donor involvement, policies on unsolicited findings, and suitability for industry collaboration, amongst others. Part of these topics go beyond current biobank accreditation (e.g. ISO norms). For example, being accredited as a central biobank facility does not necessarily mean that individual collections are open for collaboration with external researchers or industry.

A quality mark that combines all these different criteria would help users and other stakeholders to find biobanks and collections that fit their standards. In a recent workshop, biobanks themselves also indicated the need for such a quality mark (van der Stijl et al. 2018). However, development and implementation will not be straightforward. Determining the quality mark's criteria will require input from a wide range of stakeholders (e.g. biobankers, researchers, funders, patients) and most likely create controversy, also considering already existing and closely related or overlapping standards such as the new ISO-20387 norm. In addition, who will issue the quality mark and monitor compliance? To be successful, a long-term project owner is necessary to gather input, establish the quality mark, and drive implementation.

4.3. The Netherlands must continue to promote biobanking collaboration

Over the years the Netherlands has known many initiatives aimed to increase collaboration and reduce national fragmentation within the biobanking field. Despite the successes, many challenges still exist as users experience fragmentation on topics such as medical ethical reviewing, informed consent procedures, unsolicited findings, issuance procedures, legislation, and automation (e.g. electronic health records, laboratory management systems). This fragmentation is partly because the involved Dutch institutions cannot agree on a harmonised policy or approach; everyone prefers to stick to their own approach. One underlying cause is the competition between individual university medical centres.

[6] Real world data is data derived from sources associated with outcomes in a heterogeneous patient population in real-world settings. Such sources could be electronic health records, claims and billing activities, product and disease registries, etc. Real world data is opposed to data gathered in a controlled experimental setting such as a randomized controlled trial.

[7] A personal health environment is a digital platform in which citizens can keep track of, manage, and share their health data gathered by different health organisations (e.g. hospital, general practitioner, laboratory, physiotherapist). Citizens can also add data they have collected themselves (e.g. smart watch).

This lingering fragmentation limits the potential impact of biobanks for research and health care as it results in lengthy issuance procedures and confusion on the side of both biobank and user. As biobanks or biobank-related research projects often cover more than one institute, and each institute has its own policies, users have to reach agreement with each separate party before samples and data can be issued. This process causes frustration and may lead to projects being cancelled altogether.

The Netherlands must continue to promote national cooperation within the biobanking field to tackle these unresolved issues. In addition, instead of competing against each other the Dutch medical centres should compete against other countries for public and private funding. Strong nationwide collaborations and coordinated, streamlined policies would greatly increase the accessibility and potential impact of Dutch samples and data.

4.4. BBMRI-NL: expectations versus reality

What became clear from the focus groups is that academic biobank users have expectations from BBMRI-NL that do not always align with what BBMRI-NL is able to offer in reality. Users expect BBMRI-NL to facilitate local biobanks, similar to an industry association, with a main focus on addressing overarching topics that individual biobanks are not able to solve on their own. Such topics would include the linking of biobanks and datasets across the Netherlands; creating a clear overview of available biobanks, samples, and data; and standardising data, agreements, policy and legislation. The envisioned role would then more closely resemble the German BBMRI equivalent, the German Biobank Node, which consists of a collaborating network of local biobank facilities supported by a central national office focused on joint issues.

In reality, BBMRI-NL is a research infrastructure with the mission to maximize the use of samples, images, and data for health research on the prevention, diagnosis and treatment of diseases. And as a research infrastructure, BBMRI-NL aims to serve and collaborate with many different stakeholders. For example, for researchers, BBMRI-NL provides sample and data catalogues, centralised access to a number of the Dutch collections, research tools, a number of unique multi-omics collections, and ethical and legal support. For biobanks BBMRI-NL provides several services such as a public website, a biobank registry, a platform for patient and donor interaction, efforts to link biobanks and medical registries, privacy compliance tools, guidelines on a number of topics, and an international representation role. Involving all different stakeholders is crucial to reach the envisioned goals. To avoid a mismatch between expectations and reality, BBMRI-NL should communicate more clearly towards all stakeholders what their mission and vision is and what goals they are pursuing.

5. Next steps

Improving the use, impact, and sustainability of biobanks requires effort from all stakeholders involved. The results from these focus groups will be combined with the input gathered from biobanks themselves (van der Stijl et al. 2018) to create stakeholder-specific recommendations. These recommendations will serve as a starting point for discussions with funders, patients, policymakers, and other stakeholders; on setting suitable overarching Dutch prerequisites. Only through joint action can we create a macro-environment that enables and promotes sustainable biobanking; for the benefit of medical research, health care, and the Dutch population.

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7. Appendix

7.1. Questionnaire focus groups academic researchers (English)

Questions part 1: Biobanks in general

1. Could you give a short introduction about yourself (function, type of research), which biobanks you use, and if these samples and/or data are gathered by your research group or collected by another/third party?
2. Imagine that all biobanks in the Netherlands close, what would be the consequences? (in other words: Why are biobanks needed?)
3. What do you expect from a biobank?
4. What are important preconditions a biobank must have in place?
5. What are the most important problems or obstacles that you currently experience as user?
6. When would you use samples and data from an existing biobank (a third party/outside the own research group) instead of collecting the samples and data yourself?
7. Financing of biobanks is a tough subject. What is your opinion about this?
    a. When would you, as a user, be willing to pay for samples, data and/or services from a biobank?
8. Imagine, you are responsible for improving the Dutch biobank infrastructure as a whole, what would be the first thing you tackle?

Questions part 2: Location specific

1. How do you know the [CENTRAL BIOBANKING FACILITY/INSTITUTE]?
2. What are your expectations of the [CENTRAL BIOBANKING FACILITY/INSTITUTE]?
3. What are your experiences with the [CENTRAL BIOBANKING FACILITY/INSTITUTE]?
4. How can the services of the [CENTRAL BIOBANKING FACILITY/INSTITUTE] be improved?
5. What are future needs that the [CENTRAL BIOBANKING FACILITY/INSTITUTE] must respond to?
6. Imagine, you have one minute to talk about this subject with the director of the [CENTRAL BIOBANKING FACILITY/INSTITUTE], what would you say?

7.2. Vragenlijst focus groep academie (Dutch)

Vragen deel 1: Biobanken algemeen

1. Korte introductie over jezelf (functie, onderzoek), van welke biobanken je gebruik maakt, en of deze samples/data door je groep zelf zijn verzameld of door een derde/andere partij?
2. Stel dat alle biobanken in Nederland wegvallen, wat zou dat voor gevolgen hebben? (in andere woorden: Waarom zijn er biobanken nodig?)

3. Wat verwachten jullie van een biobank?
4. Wat zijn dan belangrijke randvoorwaarden waaraan biobanken moeten voldoen?
5. Wat zijn de belangrijkste problemen en/of obstakels die jullie op dit moment ervaren als gebruiker van biobanken?
6. Wanneer zouden jullie gebruik maken van samples en data uit een bestaande biobank (van een derde partij/buiten de eigen onderzoeksgroep) i.p.v. deze zelf te gaan verzamelen?
7. De financiering van biobanken is een lastig onderwerp. Hoe kijken jullie hier tegenaan?
    a. Wanneer bent u als gebruiker bereidt om te betalen voor samples, data en/of services uit biobanken?
8. Stel, je bent verantwoordelijk voor het verbeteren van de Nederlandse biobank infrastructuur, wat zou dan zo snel mogelijk aangepakt moeten worden?

Vragen deel 2: Locatie specifiek

1. Waarvan kennen jullie de [CENTRALE BIOBANK/INSTITUUT]?
2. Wat zijn jullie verwachtingen van de [CENTRALE BIOBANK/INSTITUUT]?
3. Hoe zijn jullie ervaringen met de [CENTRALE BIOBANK/INSTITUUT]?
4. Hoe kunnen de services van de [CENTRALE BIOBANK/INSTITUUT] verbeterd worden?
5. Wat zijn toekomstige behoeftes waar [CENTRALE BIOBANK/INSTITUUT] op in moet spelen?
6. Stel dat je een minuut de tijd heeft om over dit onderwerp te praten met de directeur van [CENTRALE BIOBANK/INSTITUUT]. Wat zou je dan zeggen?

7.3. Questionnaire focus group private industry (English)

1. Could you give a short introduction about yourself (company, function, type of research) and how biobanking is organised within your company?
2. Who has tried to collaborate with or use samples and/or data from an academic biobank?
    a. And who succeeded?
3. What are your experiences with academic biobanks?
4. What do you want to get from an academic biobank?
   (in other words: what are you interested in? What are you looking for?)
5. What are the most important challenges or obstacles that you currently experience as user or potential user of academic biobanks?
6. What are important preconditions academic biobanks must meet to be used by companies?
    a. When are samples and data fit for purpose?
7. Financing of academic biobanks is a tough subject. Funders sometimes expect biobanks to be self-sustaining. What is your opinion about this subject?
8. The research and development field is changing rapidly. In five years' time the world will look completely different. What are future needs academic biobanks must respond to?

7.4. Vragenlijst focus groep private industrie (Dutch)

1. Korte introductie over jezelf (bedrijf, functie, type onderzoek) en hoe biobanking er binnen jouw bedrijf uit ziet.

2. Wie heeft er wel eens geprobeerd om samen te werken met of gebruik te maken van samples en/of data uit academische biobanken? (“vingers”)
    a. En wie is daarin al eens geslaagd?

3. Wat zijn jullie ervaringen met academische biobanken?

4. Wat komen jullie halen bij academische biobanken?
(in andere woorden: waar zijn jullie in geïnteresseerd? Wat zoek je bij de biobank?)

5. Wat zijn de belangrijkste uitdagingen en/of obstakels die jullie op dit moment zien als (potentiële) gebruiker van biobanken?

6. Wat zijn dan belangrijke randvoorwaarden waaraan academische biobanken moeten voldoen om door het bedrijfsleven gebruikt te worden?
    a. Wanneer zijn samples en data “fit for purpose”?

7. Financiering is voor veel academische biobanken een probleem. Funders verwachten soms dat biobanken self-sustaining zijn. Hoe kijken jullie tegen dat financieringsprobleem aan?

8. Het onderzoeks- en ontwikkelingsveld veranderd snel, over 5 jaar ziet de wereld er weer heel anders uit. Wat zijn toekomstige behoeftes waar academische biobanken op in moet spelen?