Discussion
Chapter 15

Outline

This thesis aimed to answer the main research question: How can knowledge valorisation processes in the life sciences sector be improved? by studying the following four research questions:

1. Reconnaissance: what factors hamper innovation processes across different domains?
2. Know-what: what can we learn from the articulation of unmet needs in different phases of knowledge valorisation?
3. Know-why: why do academic researchers engage in knowledge valorisation and what barriers are hampering them?
4. Know-how: how do stakeholders engage in knowledge valorisation processes and what can we learn from contextualization of process models to different fields?

In this chapter the four research questions are answered based upon the studies presented in the individual chapters. For each research question the implications for science and practice will be discussed. Furthermore, the theoretical implications of the current thesis are discussed before a reflection on the validity of this research is provided. The chapter ends with a general conclusion on the main research question.
15.1 Reconnaissance: what factors hamper innovation processes across different domains?

Chapters 4 and Chapter 5 set the scene for knowledge valorisation processes by giving a broad perspective on how collaborations between different domains facilitate or hamper innovation processes. By studying innovation barriers in two separate fields within the life sciences, these chapters provided additional insight into how barriers interact across the valorisation cycle.

15.1.1 Key findings

In each study different individual barriers were recognized and described that were specific for the field under study. The highest ranked barriers (by KOLs) for probiotics were found in the business development and market domains and reflected the difficulties with providing a sufficient evidence base to obtain regulatory approval and compete with probiotics for which no evidence base existed. In contrast, the most important barriers for rabies related to a lack of agenda setting in the society domain.

These differences are in line with the differences in technological development and market dynamics of both cases. Since the rabies market has reached its plateau of saturation, further innovative efforts are hampered by the underlying limitations of market expansion (121, 656). Despite continued unmet clinical needs, stakeholders have the impression that there is no need to further invest in rabies innovation, even though radical innovations are needed that will lead to disruptions in market dynamics (661) and solutions for the significant burden of rabies disease. Technological development for microbiota-based products is still in its growth phase and consequently innovators in this field are still developing a dominant design that is accepted by the market and conforms with demands by regulatory authorities (662). The emergence of the market (663) is reflected in the need for stakeholders to address current market failures and introduce novel value propositions that are adopted by end-users.

Whereas the ultimate barriers of both cases are highly dependent on the innovation growth phase and market dynamics of their respective fields, in both fields fragmentation across disciplinary and domain boundaries play an important role in establishing and maintaining these innovation barriers. While cross-domain collaborations are well-established for rabies (129), Chapter 4 showed that progress in the research domain is still not effectively shared with stakeholders in the business and development domain. In the emerging microbiota field, cross-domain collaborations were also found to be an important barrier for innovation. For probiotics this is most evident from the overemphasis on heterogeneous and underpowered studies in the pilot phase, referred to as ‘pilotitis’, which demonstrates that stakeholders in early phases of development lack a thorough understanding of market and society demands necessary to deliver a societal impact of new products. Interestingly, the two different cases selected for this study question a priori differed on the extent to which cross-domain collaborations were established in the field. Nevertheless, both fields were found to be hampered by barriers in such cross-domain collaborations, emphasizing its essentiality to innovation processes.
Also, in both studies fragmentation across disciplinary boundaries was shown to hamper innovation. In the context of rabies, stakeholders from veterinary and human disciplines compete for the same limited resources. This leads away from a One Health approach, which is generally considered the most efficient approach to ensure control of rabies disease. Such disciplinary differences were also seen to influence perspectives on research needs for innovation in Chapter 7. In the context of probiotics, there is significant competition, rather than collaboration, across the food-pharma disciplinary divide which hampers the integration of knowledge from both disciplines necessary to deliver on the promises of probiotic research.

15.1.2 Implications for science and practice

Both chapters demonstrated that barriers should be considered comprehensively to understand the dynamics that hinder innovation and effectively design interventions to improve the outcomes of innovation efforts. When stakeholders do not effectively collaborate across domains, innovative performance is limited but more importantly, unmet societal needs are not adequately addressed (105, 108). Moreover, innovation barriers that occur in one domain often have their root cause in another domain which leads to a cascade of causal factors that hampers innovative efforts, obviating the need for a direct (step-by-step) model. In the case of rabies this is made especially clear. The dominant rationale for limited innovation in this field is the limited return on investment which hampers involvement of stakeholders in the business development domain. The causal analysis, however, revealed that this barrier has its root causes in the society, scientific and market domains. To only focus on the barriers in one domain or on the barriers that reflect the dominant rationale would thus mean to take a symptomatic approach that does not fundamentally address the limiting factors to innovation. While tackling root causes of barriers may be difficult to accomplish due to their systemic nature, a thorough understanding of causal relations is important to consider when designing strategies to address these barriers.

The studies in Chapter 4 and Chapter 5 took a first step in understanding these relations by drawing upon experiences from different stakeholders to conduct a root cause analysis. While these chapters also suggest strategies to overcome these barriers, they did not study how stakeholders deal with these barriers in practice. Attempts to address these barriers can reveal further systemic barriers and solutions that are of importance when designing effective interventions. Especially in complex systems, probing and collaboration in addressing these barriers is needed. Further research could therefore benefit from studying stakeholder approaches to counteract these barriers in order to inform the development of measures and approaches that address barriers of a more systemic nature.

On a methodological note, Chapter 5 also emphasized the relevance of qualitative research methods to study how the barriers influence stakeholders in practice; almost half of the identified innovation barriers were only identified through the interviews and the focus group discussion, and were not yet described in literature. This further supports the rationale that a thorough analysis of barriers in the context of practice is necessary to provide a complete picture of factors that may hamper innovation to address unmet needs.
In conclusion, many innovation barriers stem from difficulties in cross-domain collaboration. These difficulties are inherent to the domain-specific discourses, methods, approaches and behaviours that are considered acceptable (99), but have different dynamics depending on the field of innovation. Additional barriers result from difficulties in collaborating across disciplinary divides. Together with field-specific root causes (e.g. interpersonal differences for probiotics and major prevalence in low-resource countries for rabies), these difficulties translate into innovation barriers that characterize the innovation landscape for specific stakeholders. To effectively design interventions that can address such barriers, a comprehensive analysis of barriers across disciplines and domains is essential.

15.2 Know-what: what can we learn from the articulation of unmet needs in different phases of knowledge valorisation?

As shown in Chapter 4 and Chapter 5, the alignment of stakeholders across domains and disciplines is a key factor in innovative performance. Such alignment can be improved by formulating joint problems and projects (664). In Chapter 6 and Chapter 7 the articulation of joint problems and projects in different phases of knowledge valorisation was explored, whereas Chapter 8 studied how alignment with unmet needs can benefit companies in an emerging market.

15.2.1 Key findings

Chapter 6-I and Chapter 6-II focused on unmet need articulation for Ebola, an emerging infectious disease. Chapter 6-I argued that mechanisms to involve stakeholders from the business development domain should entail a clear understanding of the societal unmet needs posed by emerging infectious diseases and a clear articulation of opportunities derived from these needs. Chapter 6-II revealed from the primary patent literature that such unmet needs and opportunities are not uniformly understood by different stakeholders and showed a clear mismatch in unmet need articulation by academic and industrial stakeholders: whereas industrial applicants focused on bioterrorism and neglected detection and control of nonendemic outbreaks, academic applicants did the opposite.

Chapter 7 provided even more in-depth insight in unmet need articulation and showed that formulation of research needs for rabies can exacerbate, rather than diminish fragmentation between disciplines. Key opinion leaders had widely divergent, background-specific views on the importance of, and need for improvement for the components of rabies control (e.g. animal host, human host, agent or environment). Simultaneously, Chapter 7 highlighted that addressing such societal research needs might lead to common ground between different domains and accelerate the control of rabies research. For instance, the introduction of improved and novel products may increase the impact of education and awareness programs, while accurate data on the societal and economic burden of the disease could increase political will and advocate funding for rabies control. In line with this, Chapter 8 provided a case study of organ-on-a-chip companies and emphasized the importance of hybrid business models for identifying and meeting the demands of customers. More importantly, it showed how alignment with unmet needs can lead to better
business performance in terms of marketing, access to financial resources and profit margins, while simultaneously meeting end-user demands.

In conclusion, whereas alignment in the formulation of unmet needs and opportunities can enhance collaborative efforts, in the absence of such alignment, cross-domain collaborations might be hampered even further. This leads to mismatches which are likely to result in delays and inadequacies in addressing pressing societal problems.

15.2.2 Implications for science and practice

This thesis highlighted the importance of understanding unmet needs from a more societal perspective. Knowledge valorisation is broader than university-to-industry knowledge transfer and includes activities taking place in wider society. Synchronization with unmet societal needs – including the need for curiosity-driven research – can improve the societal impact of academic research. These unmet needs can for example relate to additional target groups for the same NME or to improvements in formulation or administration of the current NME. It therefore shows that it is important to be aware of these mismatches and that clear articulation of perceived unmet needs is necessary to ensure institutional concordance among stakeholders belonging to different innovation domains. Facilitators of transdisciplinary collaborations can play an important role in this articulation (665-667).

Previous research showed that unmet needs differ between different actor groups (668). In order to fully understand the unmet needs that exist in society, inclusion of all actor groups involved is therefore necessary. The current studies have primarily focused on key opinion leaders and did not include lay or patient representatives. Future research should therefore focus on the engagement of a range of societal stakeholders for demand articulation and the role they play in the democratization of science (669, 670).

Interestingly, the articulation of research needs for rabies exacerbated existing boundaries between different disciplines, whereas the hybrid business models in the context of emerging cross-domain collaborations in the microbiota field led to alignment of expectations among companies and end-users. These findings may be explained in the context of “boundary objects” and “boundary work”. Boundary objects represent information that have the flexibility to be used in different contexts by different audiences, while maintaining their integrity (671). As such, they can ensure coherence across intersecting domains (672). In the context of knowledge valorisation, such boundary objects can take the form of articulated unmet needs to facilitate collaboration between the society and science domains, or the form of opportunities defined during the fuzzy front end of innovation to bridge divides between the science and business development domains. Boundary work, in contrast, refers to activities of stakeholders to reinforce rather than bridge the boundaries between domains. In the absence of alignment between domains, stakeholders might engage in boundary work to strengthen the borders between their respective domains, which is in line with findings on transdisciplinary team formation (665). It is therefore likely that the misalignment of stakeholders in the fields of rabies and emerging infectious diseases is preceded by previous boundary work between stakeholders (673) and further research on the effect of existing collaborations on alignment between stakeholders is warranted.
15.3 Know-why: why do academic researchers engage in knowledge valorisation and what barriers are hampering them?

15.3.1 Key findings

The engagement of different stakeholders within the valorisation cycle is important to generate societal benefits. Although this is true for all stakeholders involved, this thesis placed a special emphasis on academic researchers through studying the incentives (Chapter 9) and motivational drivers (Chapter 10) that influence their engagement. This focus is justified by the strong influence of academic engagement on the success of knowledge valorisation practices (349, 442) as shown by its step-limiting nature (335-337), and the lack of knowledge on how the engagement of academic researchers can be improved. Chapter 11 took a broader perspective and looked at barriers from different stakeholder perspectives.

Chapter 10 found that in addition to the conventional personal, professional and pecuniary drivers used in studies on academic engagement, a fourth category of moral drivers can be recognized an influence to the engagement of academics with other domains. This category of drivers is particularly relevant for two pillars of societal impact that have been underserved in previous research: impact on culture (e.g. efforts to increase public understanding of scientific progress) and impact on wellbeing (in Dutch: welzijn, e.g. efforts that contribute to development of guidelines or standards by professionals or state-governmental stakeholders).

This chapter furthermore showed that performance in the economy domain is positively associated with all types of motivation, indicating that it is a mistake to assume that engagement in product and process innovation is solely driven by pecuniary motives. In contrast, this finding substantiates the theorem that academics are only successful in this domain when they remain distinguishable from firms and don't focus merely on pecuniary outcomes, in order to fuel the virtuous cycle (458) between economic activity and academic productivity (459).

Chapter 9 showed that the distinction between firms and universities is also a point of concern when implementing incentives at universities; stakeholders were worried that incentivizing knowledge valorisation activities might come at the expense of the other two main tasks of universities: research and education. Incentives were therefore designed to serve multiple purposes within universities beyond rewarding well-performing employees. In addition to rewarding performance, incentives aimed to contribute to changes in institutional logics and create awareness and appreciation of successful valorisation activities. The most important institutional consideration, however, was found in the restricting conditions to limit potential conflicts of interest that accompanied incentives for knowledge valorisation. Although understandable from a risk management perspective, such restrictive conditions counteract the incentives they accompany and thereby might limit rather than improve academic engagement.

Chapter 11 further elucidated this by studying factors that limit engagement in research and innovation practices. Within the context of the Nagoya protocol and the importance of sharing microbial genetic resources for adequate public health responses, this chapter highlighted that two out of four barrier categories relate to ‘punishments’ for pro-sharing behaviour: negative
consequences of data sharing by actions of others and self-interest referring to opportunity costs that collaborating stakeholders might incur when engaging in collaborations to share their data. Interestingly, publication priority was the most frequently mentioned barrier, which is in line with the importance of career progression for incentives and motivational drivers highlighted in Chapter 9 and Chapter 10.

### 15.3.2 Implications for science and practice

The study into three different aspects of motivation to engage in knowledge valorisation (motivational drivers, incentives and barriers) elucidated the dual nature of the implementation of the third mission in universities: on the one hand policy measures are implemented to further academic engagement, while on the other hand, restricting conditions, opportunity costs and negative consequences hamper this engagement. This phenomenon seems to occur especially at the researcher level, which places the risks for societal engagement at a low level in the organization.

Further research should therefore consider the combination of such forces and how they influence different organizational levels, including the level of the researcher, the university and the innovation system. More particularly, further research should study whether changes to the reward system in science can contribute to engagement of researchers in knowledge valorisation processes without placing the corresponding opportunity costs primarily at the individual level.

Policy directions to address impediments to engagement of academic researchers in knowledge valorisation processes include simplified and clarified legal frameworks for engagement in collaborative data sharing efforts across the valorisation cycle, as argued for in Chapter 11. Additionally, whereas Chapter 11 suggests that acknowledgement of data sharing contributions in assessments of academic research credit can alleviate barriers to engagement, the combination of the chapters studying this sub question supports efforts that argue for acknowledging a wider variety of activities in knowledge valorisation for career progression (674).

### 15.4 Know-how: how do stakeholders engage in knowledge valorisation processes and what can we learn from contextualization of process models to different fields?

To assist stakeholders in shaping valorisation processes, the final section of this dissertation focused on the question of know-how. The studies contributing to this sub question started from a thorough synthesis of conceptual models to describe knowledge valorisation, thereby contributing to the acceptance and usability of these models by both practitioners and researchers.

#### 15.4.1 Key findings

In Chapter 12, an analysis was made of 32 different models on knowledge valorisation processes. This chapter showed that there are many different interpretations of valorisation processes. Moreover, a wide variety of possible contextual heterogeneities (for example, in terms of national
innovation systems or sector-specific regulations) makes it impossible to develop a model that accurately maps all potential situations of knowledge valorisation. Nevertheless, an actor- and domain-transcending perspective enables stakeholders to appreciate the full scope of knowledge valorisation and the full extent of the potential societal impact of knowledge. This perspective complements models that offer a more isolated and in-depth focus on subprocesses (e.g. transfer of knowledge), specific domains (e.g. the science and industry domains), or certain actors (e.g. university administrators). The synthesized model may therefore serve a boundary-spanning purpose by increasing reciprocal insight, and thus appreciation, among stakeholders across domains.

By taking this inductively derived conceptual model as an initial framework and deductively contextualizing it to the vaccine industry, the theory was tested against expert perceptions which ultimately led to the identification of industry-specific stage-gates in Chapter 13. This chapter showed that for vaccines, having reached maturity in its technological development, parallel subprocesses can be discerned and described. Some of these processes consist of defined steps, subject to sector-specific regulations, whereas the timing and occurrence of other subprocesses was contingent on contextual factors. Additionally, Chapter 13 highlighted the importance of understanding the criteria that are employed in different phases and different domains of innovation, for progression along the innovation value chain in established cross-domain collaborations.

Chapter 14 further elaborated on the synthesis of conceptual models in Chapter 12 by providing activity and sub-activity descriptions for each of the phases and domains derived from literature. This general description of activities can serve as a starting point for involved stakeholders to understand and reflect on the activities within the different domains important for knowledge valorisation. With the microbiota field being in the growth phase of technological progress, the synthesized conceptual model was not translated to industry-specific stage-gates but rather eight key points for successful innovation were captured based upon experiences by early innovators.

### 15.4.2 Implications for science and practice

The inductively derived conceptual model can be used as a framework to describe and understand valorisation processes in general. This will enable innovation stakeholders to shape and accelerate progress across the value cycle. Exact activities within specific fields and within specific innovation projects will remain contingent on contextual heterogeneities and therefore contextualized models will differ from each other. In this sense, the societal impact value cycle serves as a heuristic tool to facilitate knowledge sharing. Importantly, it doesn't share the tacit knowledge that practitioners have accumulated in practice (675) and should therefore not be mistaken as a tool to replace tacit knowledge sharing. Rather, it serves as a means to facilitate collaboration, mutual understanding and knowledge sharing across boundaries.

As highlighted in Chapter 14, processes in the society and market domains are underrepresented in current conceptual models, while they lead to a range of innovation barriers, as shown in Chapter 4 and Chapter 5. These processes are even harder to delineate than processes within
the other domains, since these are influenced by a range of societal and political dynamics. Nevertheless, considering their importance for progress along the demand-driven value chain, as shown in Chapter 6 and Chapter 7, further research should study the role of these domains in valorisation processes.

15.5 Theoretical implications

This thesis started with the combination of two theoretical models that have often been described as being in contrast to each other: the linear model of innovation and the systems of innovation perspective. Taking a weak interpretation of the linear model, rather than the strong interpretation that is often used as a straw man model, this study shows that the description of innovation processes is of value for understanding innovation dynamics. By linking the description of innovation to the systems of innovation perspective it elucidates how different phases are shaped by the contexts in which they are typically executed. Importantly, while the systems of innovation approach serves primarily to inform policy decisions on how to support the performance of such systems (676), the current Societal Impact Value Cycle serves as a means for individual stakeholders to facilitate mutual understanding and collaboration in shaping innovations.

The current thesis highlights that specific steps in innovation systems are executed by different actors, depending on personal and contextual factors. The differences in the contextual background of stakeholders might influence the timing and rigidity with which some activities are executed, as highlighted for manufacturing in Chapter 13. Simultaneously, the institutional constraints and possibilities of the domain to which the phase belongs are important in shaping stakeholder activities, and vice versa these activities shape the constraints and possibilities. Scientific research can for instance be conducted by different stakeholders. The two most prominent stakeholders, academia and industry, both contribute to the Academic Response Repertoire (90) which can be seen as the capabilities developed to respond to future demands. Innovation is then defined as the development of novel products, services and processes through new combinations of these capabilities. In Chapter 13, the involvement of different stakeholders in research phases becomes evident for the vaccine industry. In Chapter 14, the importance of including societal stakeholders in early phases of innovation is further elucidated by outlining their influence on innovation success. Importantly, Chapter 9, Chapter 10 and Chapter 11 show that to facilitate engagement of stakeholders across the value cycle, drivers and incentives should be evaluated within the institutional context in which these stakeholders operate.

Despite the importance of networks of actors for effective knowledge valorisation processes (677), this thesis did not study the know-who dimension of knowledge. Know-who deals with the social capital of people that can be used to acquire and leverage other knowledge components (112) and is highly contingent on contextual factors (114). Depending on the specific context, different value networks consisting of stakeholders from different systems contribute to valorisation processes. These include public-private partnerships, open innovation programs, centres of excellence, etc. (71). A more in-depth study on these value networks can therefore add a third dimension to the valorisation cycle, showing which stakeholders contribute to the different phases.
Next to the structural aspects of innovation systems, as defined by actors, their institutions and the networks they form, innovation systems can be characterized by a number of processes, which are conceptualized as functions (102). Seven functions that have been described are: guidance of the search; knowledge development; knowledge diffusion; entrepreneurial activities; mobilization of resources; creation of legitimacy and market formation (102). Innovation systems are often mapped in terms of how well and in which order specific functions are met in order to study innovation barriers and inform policy decisions on a system level (678). This approach, however, does not provide stakeholders within the innovation system with an understanding on how they can themselves contribute to improved innovation effectiveness.

The current thesis therefore combined the systems of innovation perspective with a weak interpretation of the linear model of innovation to facilitate understanding of innovation dynamics among stakeholders involved in knowledge valorisation. This leads to a conceptual refinement of some of the functions of the systems of innovation which are reflected upon below. Here, it is also important to re-emphasize that the SIVC does not include policy measures that influence valorisation processes. Rather, these policy measures can be seen to interact with all individual phases and domains within the SIVC.

The first function of innovation systems is guidance of the search, which is defined as the selection of loci for innovation. This function is in line with demand articulation, which takes place in the society domain. Importantly, this thesis extended this function with the understanding that demand articulation is preceded by identification of unmet societal needs. Many different actors contribute to unmet need identification and demand articulation, including industry, governments and market stakeholders, and the current research highlighted how aligning these needs and demands can lead to the generation of boundary objects that improve collaboration.

A second function of innovation systems is knowledge development. Whereas this is often described to include not only technical knowledge, but also other types of knowledge such as market or production knowledge (676), the SIVC distinguishes between knowledge creation that aims to enhance understanding and knowledge development that aims to apply and improve existing knowledge, in line with other scholars on the topic (84). All knowledge creation that aims to enhance understanding, whether it is use-inspired or not, is conceptualized as research occurring in the science domain. Knowledge diffusion, a third function of innovation systems, then takes place within the science domain or between the science domain and other domains. In some cases, this knowledge diffusion is formalized via intellectual property protection and transfer processes which enable actors in the business development domain to generate a return on their investments.

Entrepreneurial activities take place within the business development domain, where new entrants or incumbent companies experiment with new technologies, applications and markets to deliver new value propositions to the market (102). The current thesis refined the description of these activities in technological development, commercial development, and production and upscaling (see Chapter 12). Contextualizing the SIVC to the field of vaccines in Chapter 13 enabled further refinement of these activities.
The mobilization of human and financial resources is of interest for research and development activities in different domains. Indeed, the conceptual models analysed in Chapter 12 and Chapter 14 describe the resourcing of research in the scoping and preparation phase, and the resourcing of business in the commercial development phase. Contextualization to the vaccine field in Chapter 13 highlighted that the mobilization of resources takes place multiple times during innovation processes.

The last two functions described in the context of innovation systems are the creation of legitimacy and market formation (102). Market formation in the context of innovation systems deals with analysing the timing, size, type and development of markets in order to design policy approaches to address difficulties with market introgression, for instance by establishing niche markets or introducing tax incentives. In contrast, the current thesis elucidates that innovators themselves can also play an important role in facilitating market adoption, as highlighted in Chapter 13 and Chapter 14.

Market formation is supported by activities that support the social acceptability and endorsement of their activities within their institutional context and beyond (679), a function known as creation of legitimacy. A subtype of legitimacy, regulatory or socio-political legitimacy describes the compliance of stakeholders to formal rules, laws and regulations and thereby their interface with the policy domain (679). Although these activities are not described in the inductively synthesized SIVC presented in Chapter 12, they are part of the contextualized VIC in Chapter 13 where they are referred to as public affairs.

The current thesis therefore refines the functions described in a systems of innovation perspective. The combination of the systems of innovation with a weak interpretation of the linear model led to the development of the SIVC. This model provides insight into the iterative and parallel nature of innovation processes, the distinction between radical and incremental innovation, the function of unmet need identification and demand articulation and the importance of use-inspired basic research, as outlined below.

The execution of activities described in the SIVC should not be seen as a one-directional pipeline with a fixed sequence of steps. Rather, the steps within the cycle are iterative, can be executed in parallel and include many feedback and feed-forward loops. In Chapter 13 the parallel nature of different stages and gates is further elaborated for the vaccine industry. Here, 29 distinct stages and 28 corresponding gates are clustered into ten separate workstreams that contribute to the contextualized Vaccine Innovation Cycle. It also shows that whereas some steps are more defined, the occurrence and timing of other steps are dependent on contextual factors and yet other steps take place in a continuous manner.

Importantly, activities and functions of innovation systems influence and reinforce each other. The Societal Impact Value Cycle elucidates these reinforcing influences by highlighting that innovation processes should not be seen as value chains, but that innovation takes place in a cyclical manner. As with a Deming cycle, new innovations build upon existing knowledge, upon entrepreneurial activities, and upon introductions of new innovations in niche markets that refine demand articulations in a continuously improving manner. From a contrasting perspective, and in line with the systems of innovation perspective (102), this thesis showed that
when functions are not fulfilled, a vicious cycle can emerge in which functions are not reinforced but like in the probiotic industry lead to the arrest of the innovation cycle (see Chapter 4).

In contrast to the systems of innovation perspective and the linear model of innovation separately, the SIVC that builds upon both models in a cyclical nature can additionally be used to conceptually distinguish radical and incremental innovation processes, as elaborated on in Chapter 13 and Chapter 14. When stakeholders continue in new iterations of the cycle for the same product-market combination, such iterations lead to incremental innovation (120). When incremental innovations are taken through the value chain, many steps can be copied from the previous loop or information that was obtained in the previous loop can be used to speed up the current process (96). These incremental innovation loops can be maintained until technology saturation is achieved. In contrast, radical innovation that creates novel product-market combinations build on discontinuities in terms of marketing and/or technology and can therefore originate from any place in the cycle (656). When unmet needs refer to a completely new innovation, for instance a new therapeutic area, a radical innovation is necessary. In these cases a new value cycle is started and every step needs to be taken again in full (680). The organ-on-a-chip companies studied in Chapter 8 combine both radical and incremental innovation approaches by incrementally improving their services to respond to unmet customer needs while simultaneously building upon technological discontinuities to develop really new or even radical products.

To emphasize that demand articulation is often a driver for virtuous cycles, during this thesis the valorisation cycle was rotated and in the final Societal Impact Value Cycle unmet societal needs are placed on top. Importantly, as was shown in Chapter 4 and Chapter 5, key opinion leaders emphasize the need for use-inspired basic research to contribute to innovation, such as viral pathogenesis and immune system responses in the case of rabies and the mode of action of probiotics in the case of probiotics. Chapter 7 further elaborates on this by showing that societally articulated research needs are not restricted to fundamental understanding of the rabies virus in the laboratory setting, but include needs for understanding the disease in the context of application. These results emphasize that it is not sufficient to merely focus on translation of research results from curiosity-inspired basic research to clinical development, and from clinical development to clinical adoption (55). Indeed, many of the innovation barriers and unmet research needs found in Chapter 4, Chapter 5 and Chapter 7 do not exist within the confinements of the laboratory or controlled clinical trial setting, but are part of the practice-based setting. Therefore, stakeholders within the science domain (e.g. academic researchers, funders and university administrators) should pay increased attention to use-inspired research based upon a range of unmet societal needs as captured and formulated by societal stakeholders (681). Next to the societal need for curiosity-based research this includes the need for practice-based research that studies medical interventions in the context of application (58). Such practice-based research can then contribute to the implementation of new medical interventions, inform new clinical questions and potentially challenge conventional assumptions underlying common research practices (682). There thus is a need for a broad and structural articulation of unmet needs.
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Chapter 6 and Chapter 7 highlight the importance of use-inspired basic research and in combination with Chapter 9 and Chapter 10 show how alignment with unmet needs and engagement in innovation efforts does not necessarily result in less fundamental research. In this sense it is important to emphasize that use-inspired research is not necessarily less fundamental than research that is conducted without any considerations for its use (84). The arguments from some scholars that universities should be wary to not drift away from their mission of conducting basic research (683) is reflected in the restricting conditions that accompany incentives for knowledge valorisation, as shown in Chapter 9. Nevertheless, Chapter 10 emphasizes that the basic or applied nature of research does not influence performance or effort in the economy domain. Indeed, engagement in use-inspired research was seen to even improve fundamental research outputs, leading to reinforcing interactions between academic and societal output (684). As such, this thesis suggests that the applicability of research is not a pressing factor on knowledge valorisation per se, but rather influences the type of valorisation activities that researchers are most likely to engage in.

It can even be argued that the conduct of pure curiosity-based research without being informed by unmet needs can only be justified if this research is executed by brilliant scientists, who are likely to generate results that benefit society in serendipitous (107) and anachronistic ways. In this respect, it makes sense to focus on the need for excellent science, rather than on basic science. Indeed, excellent science has been shown to positively influence scientific and economic impact (685). Whereas the knowledge paradox suggests that Europe’s high quality scientific output is not translated into similarly high quality innovative performance (686), the existence of this paradox has been debated in recent years. Indeed, it seems that not only the limited capabilities for innovation of European companies, but also the limited excellence of basic science contributes to the existence of this paradox (69, 687). To effectively improve the innovation performance of Europe, investments in excellent science are thus considered essential. This includes the reproducibility of academic preclinical drug discovery (76). The establishment of the European Research Council (688) and the increased prominence of performance-based funding across European nation states (689) are promising initiatives to elevate the quality of European science. When stakeholders from the science domain additionally collaborate with stakeholders from the industry domain in conducting this excellent science, the research outcomes can more easily be translated in successful innovation efforts (62).

In conclusion, the combination of a systems of innovation perspective with a weak interpretation of the linear model, does not only inform policy makers on the nature of barriers, but simultaneously provides stakeholders with an understanding of how they themselves can contribute to improved innovation effectiveness. In this sense, the current thesis shows that a weak interpretation of the linear model of innovation is not at odds with a systems perspective of innovation. Rather, a combination of the two models is of added value for facilitating understanding of innovation dynamics among stakeholders and policy makers. The SIVC developed in this thesis demonstrates how a structural approach to innovation can elucidate important steps and evaluation points in valorisation processes. Early identification of bottlenecks can inform approaches to address them and thereby improve and accelerate valorisation processes. By advancing the linear model into a circular model, reinforcing activities are elucidated and stakeholders are enabled to contemplate the incremental or radical nature of their innovation.
15.6 Validity

This thesis took a multiple-case study approach to study how knowledge valorisation processes could be improved. This enabled the exploration of polar cases, in terms of technological and market development and in terms of the existence of cross-disciplinary and cross-domain collaborations. This led to differences and similarities in findings per study, as outlined above, and provided a broad understanding of knowledge valorisation processes within the life sciences.

Combining qualitative and quantitative methods, this study aimed to test qualitative research findings in a broader setting (e.g. in the studies that used prioritization in surveys) and, vice versa, to qualitatively understand the underlying dynamics of quantitative results (e.g. for understanding the influence of motivational drivers, incentives and hybrid business models). With these methods, this study depended upon the co-creation of knowledge with a wide variety of stakeholders. These stakeholders included representatives from the different domains involved in knowledge valorisation who had extensive experience in their respective field (e.g. vaccines, microbiota, emerging infectious diseases and rabies). This led to a qualitative understanding of the practical aspects of knowledge valorisation processes, which further enhanced the external validity of this thesis. Moreover, the external validity was improved by comparing findings with extant literature on multiple occasions (151).

Next to method triangulation, the studies in this thesis were also based upon researcher triangulation, with multiple researchers being involved in the design of the study, data collection, analysis and interpretation. The main researcher in all of these studies has been personally engaged in knowledge valorisation processes and extensive discussions with stakeholders beyond the academic peer community over the course of this thesis as well to enhance the social robustness of the research findings (669). Other researchers had no practical experience in knowledge valorisation. This combination enabled the research team to explore rival explanations which were thoroughly discussed to improve data analysis and improve understanding.

Whether the results, and especially the conceptual model, are also transferable to other disciplines and sectors, beyond the life sciences, has been extensively debated during the course of this thesis. A clear example is the understanding of the market domain, which is here conceptualized as the context in which new products, services and processes are implemented to be used by specific stakeholders. Discussions with stakeholders in the humanities sparked resistance to this conceptualization since they felt this referred to a commodification of their knowledge. On the other hand, they were enthusiastic about the use of their knowledge by the general public, for instance in the form of books or presentations. These discussions highlighted the importance of vocabulary and how different phrases have different meanings in different contexts. The importance of the syntactic quality of the valorisation model also became evident during the contextualization of the model to the field of vaccines. The terms initially used in the Societal Impact Value Cycle defined in Chapter 12, were adapted to fit vaccine sector jargon in the development of the Vaccine Innovation Cycle. For example, in contrast to initial labels such as “Scoping”, “Research” or “Technical development”, practitioners preferred the phrases “Exploration”, “Discovery” and “Clinical development”, respectively. When applying the findings of the current thesis to broader context, the importance of the vocabulary should therefore not be underestimated (520).
15.7 In conclusion

This thesis has elucidated how knowledge valorisation in the life sciences can be improved by investigating what we can learn from unmet need articulation in different phases of knowledge valorisation, why academic researchers engage in valorisation and how stakeholders collaborate across the value chain.

Answering the know-what question, this thesis finds that the articulation of unmet needs in different phases of knowledge valorisation is not complete without the inclusion of a range of stakeholder perspectives. Stakeholders’ perspectives do not necessarily align with each other and misalignment can contribute to limited collaboration. Articulating and tackling research needs from a comprehensive perspective thus has the potential to introduce a mutually reinforcing cycle which accelerates and aligns engagement from stakeholders across the valorisation value chain. This thesis therefore argues for structural thinking to articulate unmet needs in order to contribute to progression across demand-drive value chains.

Looking into the know-why dimension, this thesis supports the rationale that motivational drivers, incentives and barriers are all influenced by the dominant norms, values and rules that determine which activities are considered legitimate and desirable within the institutional context of stakeholders. In the context of knowledge valorisation, where academic stakeholders are asked to engage with activities in adjacent domains, conflicts in these drivers, incentives and barriers occur. Next to rewarding activities that are contributing to their domain, domain-specific rules also punish activities that do not directly contribute to the domain but are valuable for the innovation system as a whole. As a conclusion, this thesis therefore finds that the engagement of academic researchers and other stakeholders should be contemplated within the context of the system they operate in.

The know-how dimension of the main research question is summarized by eight key points for successful innovation in the microbiota industry. Adding to these key points with the conclusions from the know-what and know-why dimensions, the main research question can be answered as follows: to improve knowledge valorisation processes in the life sciences sector, stakeholders across the valorisation value cycle should take the following ten lessons into account:
### Ten key lessons on how to improve valorisation processes in the life sciences sector

1. Structural thinking to articulate unmet needs is needed for progression across demand-driven value chains.
2. Effective knowledge generation requires awareness of societal unmet needs.
3. Incorporation of heterogeneous stakeholder perspectives is an early driver of successful innovation.
4. Contextual consideration of broad IP protection is essential for further development of new products.
5. Investments in absorptive capacity by industry players will advance the academic domain and translate into novel products and services.
6. Upstream and downstream contributors to innovation should collaborate instead of merely communicate.
7. The end-user’s perspective should be leading in technical development.
8. Market introgression strategies should be implemented during, and not after, technical development.
9. The societal impact of innovations will not improve without capturing and addressing market feedback.
10. Engagement of academic researchers and other stakeholders should be contemplated within the context of the system they operate in.