National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

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Foresight Studies at the Centre for Health Protection

A checklist document for foresight studies

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"It ain't what you don't know that gets you into trouble.
It's what you know for sure that just ain't so."
(Charles F. Kettering)

Preface

This advisory report has been written during a six month internship at the Dutch National Institute for Public Health and the Environment (RIVM) in the context of the specialisation Science, Business and Policy from the master programme Biomedical Sciences at the University of Groningen.

I have chosen this particular internship because I have always been interested in new scientific and technological developments, and how these developments can affect society. Foresight studies attempt to address these kinds of questions, with the goal to prepare society and policymakers for potential future eventualities. This internship allowed me to explore the theory behind foresight studies and assist the RIVM in improving their foresight performance. In addition, by selecting nanomedical devices as a case subject I could stay close to my own background and dive into a new and exciting technological field that will likely impact future healthcare and society.

During the project, focus was mostly on how foresight studies are designed, and how the Centre for Health Protection and the RIVM as a whole can improve in this regard. It became apparent that the foresight knowledge and experience within the RIVM was not fully utilised because of limited internal cooperation. One of the proposed solutions, an internal knowledge network of foresight practitioners, can amend this.

An internship is always a team effort. Therefore, I want to acknowledge the contributions of a number of people. First, I want to thank my direct supervisors, Connie and Robert, for their time and encouraging attitude. I could always drop by when I had any questions. I appreciate the fact that they gave me the space to follow my own ideas and made me responsible for my own project. I would also like to thank my supervisors from Groningen. Patrick for his critical feedback, which allowed me to improve my knowledge on nanotechnology, and Albert-Jan for his reflections, difficult questions and positive encouragement, which allowed me to grow as a person.

In addition, I want to thank a number of RIVM staff members. First, Korienke Smit for her enthusiasm and discussions. Second, Jeanne van Loon for keeping me on edge with her critical questions. Third, Leendert Gooijer and Cornelle Noorlander for their input regarding the checklist document. And fourth, Hans van Oers for enthusiastically adopting my idea for organising a gathering of RIVM foresight practitioners to start the formation of an internal network.

I want to acknowledge Ellen Willemse (Study Centre for Technology Trends) and Patrick van der Duin (University of Delft) for their time, fresh outlook and feedback on the checklist document. The checklist document and the Excel-tool rely heavily on already existing work on foresight studies. Therefore, I would like to express my gratitude to the authors of the articles, websites and documents that form the basis of the checklist document.

Finally, I would like to thank my fellow students, both at the University of Groningen and at the RIVM. The feedback sessions in Groningen helped to improve my report. Furthermore, the students at the RIVM made my time so much more enjoyable, with our timely coffee breaks and Friday market visits.

Kind regards and happy reading,

Rogier van der Stijl

Utrecht, 6th of July 2015

Executive summary

To provide the government with adequate advice the Dutch National Institute for Public Health and the Environment (RIVM) has to stay up-to-date and even try to anticipate new developments within the domains of public health and the environment. Studying the future in a proactive manner by conducting foresight studies can prepare the RIVM and their clients for potential future developments. The Centre for Health Protection (GZB), one of the centres located at the RIVM, regularly conducts foresight studies. GZB is currently looking for ways to improve the quality of their studies.

Report part 1

Problem 1: GZB uses an unbalanced mix of foresight methods
Recent GZB foresight studies use expert- and evidence-based methods, but do not use creative and interactive methods. Not using the full palette of foresight methods results in an unbalanced foresight study design. GZB foresight studies are performed behind a desk, without reaching out to citizens, stakeholders and society. This approach does not fit with the RIVM policy of moving from the side-lines to the centre of society. By staying reactive and not actively connecting to society, there is a higher chance of missing important societal developments.

Problem 2: No overarching foresight structure
Other centres and departments within the RIVM have experience with creative and interactive foresight methods. However, the lack of an overarching foresight structure poses a problem. As a result, it is difficult to find other foresight practitioners to gain advice and share experiences. It is unclear who performs which studies and has experience with which methods. The result is restricted cooperation and limited knowledge transfer between departments and centres, a general issue at the RIVM. Consequently, many foresight practitioners are on their own isolated island and have to reinvent the wheel when performing a foresight study. Improving this inefficient process can contribute to the overall quality of RIVM foresight studies.

Recommendation 1: Use more interactive methods
GZB should use interactive and creative methods in their foresight studies to gain a more balanced method mix. In addition, the use of interactive methods will result in better alignment of GZB with RIVM corporate policy, as interactive methods are an excellent tool to connect to society, promote internal and external cooperation, update mental models, and create a proactive and learning environment.

The client often determines the objectives of RIVM foresight studies, and the choice of methods depends on these objectives. For GZB to use more interactive methods they will have to convince the sponsor of their importance related to RIVM policy and their added value to individual and organisational learning, network formation, and better insight in the societal forces shaping future (technological) developments, resulting in improved anticipatory advise for the client.

Recommendation 2: Start an internal knowledge network

The RIVM should promote foresight knowledge diffusion and interdepartmental collaboration by creating an internal knowledge network of foresight practitioners. This will allow foresight practitioners to find and connect with each other, share experiences and problems, and gain advice. In addition, a network assists in creating a proactive foresight culture. The intended increase in knowledge diffusion and collaboration will result in improved individual and organisational learning. This will lead to more efficient and higher quality foresight studies, improved foresight expertise, a strengthened reputation, and possibly more external assignments. Starting an internal knowledge network can count on the support of both upper management and RIVM foresight practitioners.

RIVM should organise a meeting with all RIVM foresight practitioners to discuss the start of the internal network. By actively engaging the intended users and asking how they want to shape the network, commitment to maintaining the network is increased. The recommended network will only be successful if there is enough support and commitment from the RIVM foresight practitioners. An enthusiastic chairperson that is willing to pull the network is critical.

As stated above the foresight practitioners should themselves decide on how to shape their network. However, it is recommended to start a LINK community to find each other and easily exchange documents. Another recommendation is to organise presentations on finished RIVM foresight studies among the network members. This allows foresight practitioners to actively interact, ask questions, and provide and receive feedback with the goal of increased individual learning and the improvement of RIVM foresight studies.

Recommendation 3: Develop a checklist document and method selection tool

In addition to an internal knowledge network, RIVM should draft a checklist document for designing foresight studies, combined with a tool for selecting foresight methods. Such a checklist and selection tool will assist foresight practitioners in designing their foresight study. It will prevent groups from having to reinvent the wheel by providing them with clear handholds to design their study, hereby saving time and increasing quality.

Report part 2 & 3

Part 2 of this report contains an extensive version of the recommended checklist document (a compact working version of the checklist document can be found in appendix 3). The checklist document and the method selection tool provide the foresight practitioner with handholds for the design of their foresight study (the method selection tool is available as a separate Microsoft Excel file). The document forces the foresight practitioner to consider and answer important questions related to their study, hereby making sure that essential steps are not forgotten and decisions are made explicit. In addition, the checklist document promotes an active discussion on study design between the foresight practitioner and the client. In part 3 of this report the checklist document and method selection tool are used to design a foresight study on nanomedical devices.

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List of abbreviations

EFMN	–	European Foresight Monitoring Network
GZB	–	Centre for Health Protection
IGZ	–	Dutch Health Care Inspectorate
IPCC	–	Intergovernmental Panel on Climate Change
NB	–	Notified Body
nm	–	Nanometre
NMDs	–	Nanomedical devices
RIVM	–	National institute for Public Health and the Environment
SBP	–	Science, Business and Policy Master program at the University of Groningen
SCENIHR	–	Scientific Committee on Emerging and Newly Identified Health Risks
STI	–	Science, Technology and Innovation
STT	–	The Netherlands Study Centre for Technology Trends
VWS	–	Dutch Ministry of Health, Welfare and Sport

Project introduction

Background

One of the main tasks of the National Institute for Public Health and the Environment (RIVM) is to support policymaking at multiple government departments and Ministries with reliable and independent information and advice. To provide the government with adequate advice the RIVM has to stay up-to-date and even try to anticipate new developments within the domains of public health and the environment. Studying the future in a proactive manner by conducting foresight studies can prepare the RIVM and their clients for potential future developments[5]. The Centre for Health Protection (GZB), one of 13 centres located at the RIVM, regularly conducts foresight studies. GZB is looking for ways to increase the quality of their foresight studies.

Policymakers are often interested in new scientific and technological developments, as these developments can have a high impact on policy and society. Currently, nanotechnology is one of the most important technological developments. Nanotechnology is a key enabling technology concerned with the:

> *deliberate design, characterisation, production and application of structures, devices and systems by controlling shape and size at nanometre scale (1-1000nm, adapted from[12])*

An important development is the use of nanotechnology within medicine, also called "nanomedicine", for diagnosing, treating, monitoring or preventing diseases[13]. The field of nanomedicine consists of nanomedicinal products and nanomedical devices, which, respectively, are drugs or medical devices in which nanotechnology is used. It is expected that innovations within nanomedicine will play a major role in tackling unmet clinical needs, such as cancer and diabetes[13].

Nanotechnology and nanomedicine are developing quickly and it is likely that the diversity and complexity of future generations of these products will increase. Therefore, it is important for the RIVM's role as government advisor to gain insight in the short and mid-term developments of nanomedical devices and their potential opportunities, risks, and impact on healthcare and policy. This importance is illustrated by recent questions from the Dutch Ministry of Health, Welfare and Sport (VWS) and the Dutch Healthcare Inspectorate (IGZ) on current and future developments within the field of nanomedical devices.

Objectives

This internship has three objectives, which are reflected in part 1, 2, and 3 of this report. The first objective is to study how GZB conducts foresight studies, and provide advice on how these kinds of studies can be further improved at GZB and at RIVM as a whole. Improving the RIVM's capacity to conduct foresight studies increases the RIVM's ability to support the government with solid, anticipatory advice.

The second objective is to create a checklist and method selection tool[A] to assist RIVM foresight practitioners in designing a foresight study. The checklist should help in the selection of

[A] The method selection tool is made in Microsoft Excel and is available as a separate electronic file.

appropriate foresight methods via the method selection tool. Currently, such a checklist is absent, resulting in different departments “reinventing the wheel”. The checklist has to be useful for a broad range of RIVM projects and subjects.

The third objective is to design a foresight study on nanomedical devices according to the created checklist document and method selection tool. The RIVM frequently conducts foresight studies on technological subjects to prepare and advise the government on new developments. Developments in nanotechnology and its effect on healthcare is one of these subjects.

Methods

Employee interviews, a questionnaire among RIVM foresight practitioners, internal policy documents, scientific and grey literature[B], and finished or currently running RIVM foresight projects from the period 2014-2015 were used to determine the current state of affairs surrounding foresight studies at GZB and the RIVM and provide recommendations.

The RIVM foresight projects used are shown in Table 2 and appendix 2. These studies were gathered via conversations with staff members and internet searches. It should be noted that the number of analysed foresight studies is low (GZB n=4, non-GZB n=7). It was difficult to identify recently finished or currently running foresight studies at the RIVM. Therefore, a selection bias is possible. However, all the studies used are recent and therefore relevant to analyse. Some of the studies are a collaboration between multiple centres. In such cases the study is assigned to the centre of the study coordinator.

The used questionnaire can be found in appendix 1. The questionnaire was held among a group of 13 participants, all of which are RIVM foresight practitioners. As answering statements with agree/disagree largely depends on interpretation by the reader the results should be interpreted with care. In addition, the use of statements does not leave room for nuances. The open questions in the survey allow for more elaborate answers by the participant, thus providing more valuable information.

To draft the checklist document, scientific and grey literature, and expert and employee interviews were used. The checklist also includes an Excel-tool for selecting foresight methods. 63 methods are scored on 18 different characteristics, supplemented with a general description, advantages/disadvantages, potential output, additional comments, and suggested reading. Scoring is based on scientific and grey literature, together with the author’s own insights.

For designing the foresight study on nanomedical devices the developed checklist document and method selection tool from Part 2 were used. Furthermore, information from an on-going RIVM project on nanomedical devices provided boundary conditions, such as study objectives, available resources (e.g. time, money), and study horizon.

[B] “Grey literature stands for manifold document types produced on all levels of government, academics, business and industry in print and electronic formats that are protected by intellectual property rights, of sufficient quality to be collected and preserved by library holdings or institutional repositories, but not controlled by commercial publishers i.e., where publishing is not the primary activity of the producing body." (Definition as discussed at the 12th International Conference on Grey Literature, Prague, 2010, http://en.wikipedia.org/wiki/Grey_literature). Examples of grey literature are patents, technical reports, white papers and working papers from government agencies or scientific research groups.

Scope

The internship was performed at GZB, but is also of use for the RIVM as a whole. The checklist document and Excel-tool developed in Part 2 are to assist RIVM foresight practitioners in designing a foresight study. However, both of them might also be useful outside the RIVM. The checklist document will only focus on the design of a foresight study, and not on the implementation or finalisation. Furthermore, the checklist will not go into detail about the practical implementation of the different methods, due to the high number of methods and their flexible use. Part 3 only entails the design of a foresight study on nanomedical devices according to the developed checklist. Conducting the designed foresight study is outside the scope of this report.

Reading Guide

As stated above, the report consists of three separate parts. Part 1 includes a general introduction on foresight studies; a description of RIVM corporate policy in relation to foresight studies; an analysis of foresight studies at GZB and the RIVM; a description of the RIVM's organisational weaknesses; and a number of recommendations on how to improve foresight studies at GZB and the RIVM.

Part 2 discusses the checklist document for foresight studies and the developed method selection tool. The checklist goes into detail about project feasibility, scoping, and method selection and framework building. Finally, several take-home messages regarding foresight studies are listed. A compact working version of the checklist can be found in appendix 3.

Part 3 starts with an introduction on nanotechnology, nanomedical devices, nanomedical device regulation, and toxicity related risks. Subsequently a foresight study on nanomedical devices is designed according to the drafted checklist document and the Excel-tool, including the phases feasibility assessment, scoping and method selection and framework.

Part 1 – Foresight studies at the Centre for Health Protection

Part 1 introduces the reader to foresight studies, how these are performed at GZB and the RIVM, and how these can be improved in the future.

1. An introduction to foresight studies

1.1. Foresight to discover different future perspectives

During daily life, we constantly think about the future although often in an unconscious and automated way. The process by which people try to consider, anticipate, model, create and respond to future eventualities is called foresight[14]. Foresight studies try to approach the future in a more structured and active way, using specific methods. These kinds of studies are viewed as:

> *an action-oriented instrument for policy-making, facilitating structured anticipation, considering of alternative futures[15], requiring creative thinking and multi-disciplinary perspectives, enabling collective learning[16]; proactive and path-breaking, interactive and participatory; enabling mediation and alignment, forging new social networks, guiding strategic visioning, creating, and committing actors to shared visions[17], and supporting deliberative democracy [18].[19]*

The goal of foresight studies is not predicting the future, but the discovery and examination of different future perspectives. This is based on the idea that there is not one future but many possible futures. In addition, the future is not set; it is not an extension of the past. This allows us to make choices today that influence future developments, create new futures or prevent specific futures from becoming a reality[5].

There is no consensus on whether foresight studies should be regarded as a scientific or creative discipline. Academics and practitioners are still discussing and building the theoretical framework. As a result, foresight studies is a developing field, in both theory and practice[20-22]. This is reflected in the different names people give to the study of the future. Around the world the field is referred to as foresight studies, futures studies, futuristics, futurology or futurism[23]. In addition, there is also a broad range of different approaches or types of foresight studies. Examples are horizon scanning[24], technology forecasting[25], technology assessment[26] and scenario studies[27]. Each of these terms acts as an umbrella for a particular set of methods used during the foresight study. To simplify matters, this report refers to all different types of organised future studying activities as “foresight studies”; no matter the methods or approach used.

1.2. A broad range of objectives and topics

Both governmental and business organisations use foresight studies in their policy or strategy development process to expand the perception of available options before making a decision about the future[14]. Governmental organisations also use foresight studies to scout and prepare for future eventualities or to determine the impact of potential new developments on (different aspects of) society. On the other hand, business organisations use foresight studies to discover potential new markets and keep an eye on the competition. Thus, foresight studies can have many different objectives. The European Foresight Monitoring Network (EFMN) analysed close to 2000 foresight studies and proposed nine objective families[28] (see table 1). However, some study objectives can arguably belong to multiple families, making it sometimes difficult to classify them.

Table 1. Objective families and examples

Objective family	Examples
Actions and discussions	Development of demonstrator proposals; starting new organisations; implementing new policy
Barriers and drivers of STI	Identification of social, technological, economic, environmental, political, ethical barriers and drivers
Cooperation and networking	Creating a platform for open thinking; engaging key stakeholders at different level
Future thinking	Assessment of desired and alternative scenarios, and current visions; exploration of future trends and technologies; identification of future opportunities, threats and challenges
Grand challenges[C]	Climate change, terrorism, social equality, poverty, public health
Policy development	Advice on policy directions; new perspective on current policy-agenda and prioritisation; new guidelines for decision-making
Research/investment areas	Identification of promising technologies and markets, and successful business models; exploration of impact of potential changes in consumer demand, market share etc.
Shared visions	Evaluation of existing visions and assessment of desired, possible and alternative scenario's; creating shared visions
STI strategy/priority-setting	Setting medium-to-long-term industry goals; Determine national scientific programs;

STI = Science, technology and innovation
Objective families from [28]

A foresight study can also have multiple main and side objectives. An example is the recently published RIVM *Public Health Status and Foresight study 2014* (*Volksgezondheid Toekomstverkenning 2014*)[29], which included multiple objective families, such as orienting policy development, encouraging future thinking, generating shared visions and triggering actions and discussions. This is in contrast to a smaller RIVM study, *Lab-on-a-Chip devices for clinical diagnostics – measuring into a new dimension*[30], which had a specific focus on future thinking.

The subjects of foresight studies are diverse, ranging from the future of the legal system to new energy technologies. Different foresight studies can be classed as either vertical or horizontal studies, based on their subject. Vertical studies have an in-depth focus on a specific technology, product group, sector or geographical location, while horizontal studies are broad, include a wide range of subjects and issues and often go beyond system boundaries[5]. In addition to varying in objectives and subjects, foresight studies can also vary in size, invested resources, methods used, time horizon, geographical area and many other parameters, which will be addressed in more detail in chapter 8.

[C] A "Grand Challenge" is a major and persistent problem in a specific area that requires joint effort to solve. Examples of Grand Challenges in different areas are climate change, diabetes and poverty (author's definition).

Subjects of specific interest to policymakers are new scientific and technological developments, because of their potential impact on policy, regulations and society through the introduction of new risks or opportunities. Often the goals of technology-oriented foresight studies are to identify new trends and developments within a certain field; to identify technological areas for investment or to assess the potential impact of new technologies on societal norms and values, economy, safety, healthcare, regulations or public policy in general. Because of the potential public impact, the RIVM is often asked by government agencies to conduct foresight studies on new technological developments to gain an overview of current and potential future developments.

1.3. Different classifications for foresight methods

There are many methods available to conduct foresight studies (see for examples text box 1). Some of these methods are specific to foresight studies and consist of a specific approach, such as roadmapping and backcasting. Others are general tools or methods borrowed from other disciplines and adapted for use in foresight studies, such as brainstorming, reviewing literature and interviews. This report does not make a distinction between foresight specific methods and general tools. It rather considers all methods used in the course of a foresight project no matter if they are used to directly look towards the future or serve as orientation, support or input for other methods. From here on all activities employed in a foresight study that directly support the foresight process are considered as methods.

The prevalent opinion is that there is not one preferred method, but that each method has its strengths and weaknesses. Therefore, it is recommended to use a combination of different types of foresight methods[31-33]. The foresight studies mapped by the EFMN show an average of five to six different methods per study, although with a high variation[28]. Each method has its own characteristics, which are discussed in more detail below. However, sometimes the characteristics can depend on how the method is performed. Thus, because of the versatility of many methods and the complexity of study objectives all attempts at ordering or classifying foresight methods should be treated with caution. These kinds of classifications serve as a guide, but should not be strictly adhered to[34]. In the end, the methods used should fit the study objective and other relevant study parameters.

Foresight methods can be divided into quantitative, semi-quantitative and qualitative methods. Quantitative methods rely heavily on numerical representations. This allows for easy visualisation and interpretation of results. A downside is that, like all model systems, these methods are simplifications of reality and unable to grasp the social and political variables involved[35]. Semi-quantitative methods are concerned with applying mathematical principles to subjective data, such as expert judgements[28]. Qualitative methods are based on observations and interpretations, not on numerical values. They are often rich in information, but this information can be difficult to convey.

Popper proposed a classification based on the way methods gather and/or process information, which can be through evidence, expertise, creativity or interaction[36]. A certain foresight method combines these attributes in different quantities, although one of the four often has the upper hand. For example, brainstorming consists of ~70% creativity complemented with ~10% from the remaining attributes[28]. Popper visualised this concept in the Foresight Diamond, which displays an arrangement of several foresight methods according to this classification[36] (see figure 1).

Text box 1. Examples of foresight methods.

Brainstorming is a creative and interactive method performed in group sessions to generate a flow of new ideas around a particular subject by stimulating associations. By removing inhibitions and preventing criticism, people are stimulated to think more freely and come up with new solutions to problems. Alternative approaches are brainwriting and mind mapping.

Causal layered analysis explores the different layers of an issue, looking at empirical reality, social systems, worldviews and underlying emotive dimensions. The method moves away from linear causal determinism and investigates the subjectivity and messiness underlying social reality to enhance future thinking.

Delphi is a method consisting of a statement survey conducted in two or more rounds among anonymous participants. Results of the first round are fed back to the participants so that they can explain and re-evaluate their answers in round two. The method aims to include and structure expert knowledge while avoiding inappropriate psychological and behaviouristic effect of groups meeting face-to-face. The goal is to create consensus or clarify disagreements among experts[5].

Expert panels are knowledgeable groups dedicated to discussion and analysis of a particular subject. A panel can include all kinds of experts, which can also act as ambassadors of the foresight study. They can help in disseminating results and build network to influence decision-making[2].

Meta-analysis is an analysis of previous foresight studies and their findings. This could already provide the required answer, thereby saving the resources required for conducting your own foresight study.

Morphological analysis involves the mapping of a discipline to obtain a wide perspective of existing solutions and future possibilities through the five steps of problem formulation, identification of all parameters towards a solution, construction of multidimensional matrix containing all possible solutions, evaluation of outcomes based on feasibility and desired goals, in-depth analysis of best options.

Scenarios are a very flexible approach involving the construction and use of systematic and internally consistent visions of plausible futures. Scenarios can be created through deskwork, workshops, computer models etc[2]. Scenarios can be predictive, explorative or normative in nature.

Windtunneling is a method to test how future changes might affect the ability to deliver on a particular project or strategic objective. Participants are asked to imagine how they would meet their objectives given certain scenarios, to identify strengths and weaknesses in policy[9].

1) Creativity refers to a mixture of original and imaginative thinking and intuition resulting in the creation of something new or the improvement of something existing[5]. These kinds of methods rely on the inventiveness and ingenuity of individuals and groups[28]. Creative methods can result in fresh ideas and new points-of-view concerning possible futures. Creativity can help in leaving comfort zones and breaking dogmas. Frequently used methods with a strong creative element are brainstorming, future workshops and scenarios. Methods that almost solely rely on creativity, such as gaming, are not frequently used. An explanation could be the lack of a clear supportive conceptual and methodological framework[28].

2) Interaction-based methods bring together experts, stakeholders and lay people alike. Interactive methods are based on two considerations. First, that experts and expertise can also be found outside knowledge institutions and that this knowledge is both valuable and necessary in foresight studies. Second, that bringing together different kinds of experts, stakeholders and/or lay people in direct dialogue has a better chance of generating new ideas and thinking[5]. During interactive or participatory methods, ideas, assumptions and mental models (see text box 2) are exchanged, challenged and adjusted. Furthermore, interaction increases mutual learning and contributes to the formation of new networks[37]. Interactive methods enable democratic governance and are a way to connect to society by building public trust, generating a greater understanding of public issues, concerns, priorities and solutions, and identifying controversial views surrounding a certain issue[37]. Interactive methods should be used when the subject of a foresight study may involve unknown or

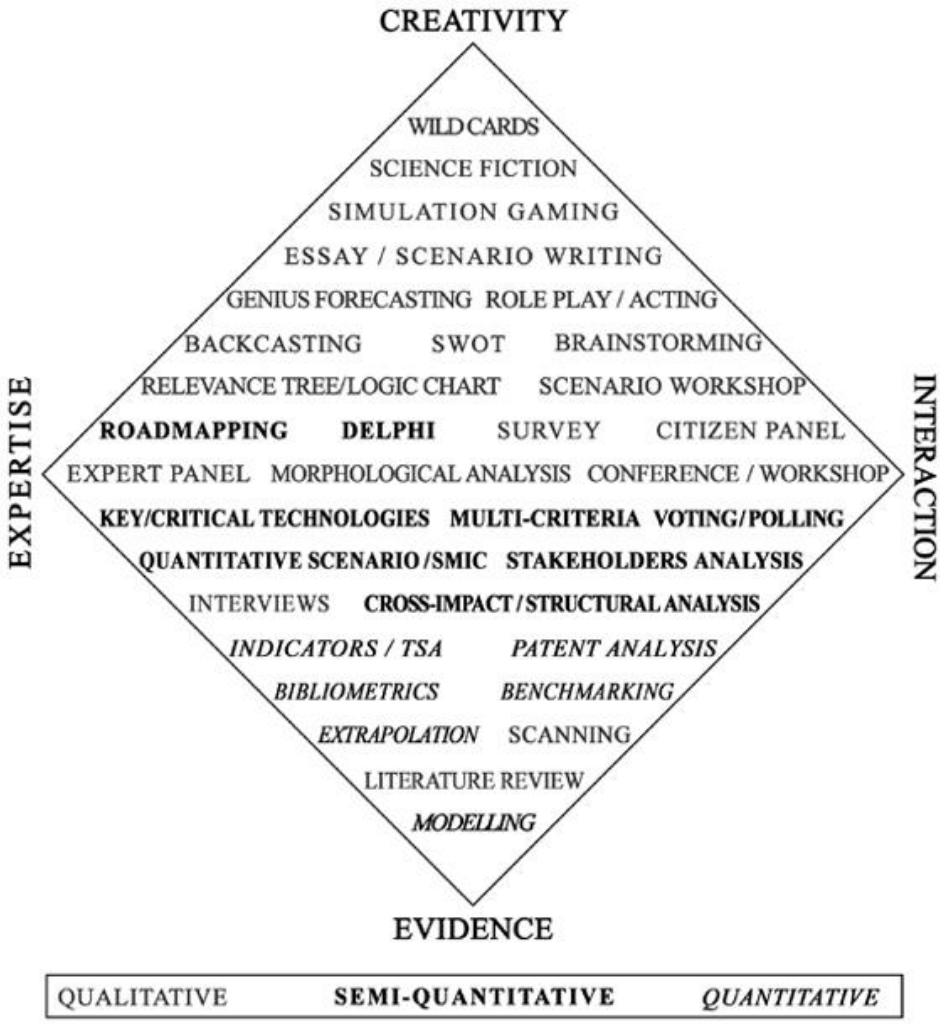

Figure 1. The Foresight Diamond. A number of foresight methods are arranged according to the proportion of creativity, interaction, evidence and expertise used in gathering and processing information. A further distinction is made based on the kind of information the method uses, which can be qualitative, semi-quantitative or quantitative in nature (adjusted from Popper, *How are foresight methods selected?*, 2008).

conflicting norms and values. Interactive methods can be difficult to organise and success depends for a great part on selection of a moderator that is both unbiased and can communicate with the different types of people involved[37].

3) Evidence-based methods attempt to explain and/or forecast a particular phenomenon by analysing codified data through well-documented methods. These methods are particularly helpful to understand the current state of affairs[28]. Furthermore, they can often be used as input for other methods. When there is sufficient reliable data on a topic characterised by limited uncertainty, it is possible to "predict" likely short-term future developments via extrapolation. Examples are population growth and ageing. However, in areas that are often affected by unpredictable events, such as technology and politics, evidence based extrapolation loses credibility and usefulness.

4) Expertise refers to the knowledge and skills of individuals regarding a particular area or subject. These individuals can be researchers, consultants, leaders of organisations or others with special knowledge in the area under investigation[5]. Expertise-based methods rely on tacit knowledge and are often used to legitimise decisions, provide advice and make recommendations[28]. Experts can summarise existing knowledge; create new knowledge; form visions; and point to new possibilities. Furthermore, experts can often informally contribute to result dissemination and follow-up activities. When selecting a group of experts for a foresight method make sure that the group has a variety of professional expertise, experience, affiliation, and personal characteristics[5].

   Experts are not necessarily good predictors of the future. A well-known example is a statement of Thomas Watson, president of IBM. In 1943, he said, "I think there is a world market for maybe five computers". At that time computers were cumbersome machines and even he as an expert could not foresee the developments in chip electronics that led to the personal computer. Like all other people, experts have subjective opinions, personal judgements and preferences, which are all a source of uncertainty[38]. In addition, experts have the tendency to be over-optimistic with respect to their own knowledge and the development possibilities within their own expertise, and a tendency to underestimate the difficulty of realising ideas[39]. However, experts are still a useful tool in foresight studies as they have in-depth subject knowledge, often an extensive network, and can provide legitimacy to the study.

There are additional classifications for foresight methods than those discussed above. Foresight methods can be predictive, exploratory or normative[40]. Predictive methods focus on one future and attempt to forecast what is going to happen, exploratory methods look forward to many possible futures and say what could happen, and normative methods look back from or towards a desirable future that should happen. Whether a method is predictive, exploratory or normative in nature can also depend on how the particular method is performed. For example, future scenarios can be made according to any of the three classifications[5].

Another distinction that can be drawn is that of diagnosis, prognosis and prescription. Diagnostic methods are concerned with understanding where we are, and therefore play a role in the beginning of a foresight study. Prognostic methods attempt to look into the future. Prescriptive methods assess what should be done and are thus concerned with making decisions. As a result, prescriptive methods are often used at the end of a foresight study.

In addition to the abovementioned characteristics, methods differ on many other aspects such as output, visualisation potential, extent to which they combine with other methods, their usefulness in uncertain and/or complex environments, the required skills, and costs, time and personnel usage.

Text box 2. How do we think about the future? – Mental models, biases and heuristics

Everyone thinks about the future according to his or her individual "mental model". This mental model is "a concentrated, personally constructed, internal conception, of external phenomena (historical, existing or projected), or experience, that affects how a person acts"[3]. It is based, among other things, on our beliefs, values and biases[4]. Research indicates that two different interacting cognitive processes are central in controlling our behaviour and decision-making, and in generating our mental models[6]. In literature, these cognitive processes are known as System 1 and System 2[7-8].

System 1 is unconscious, fast, automated, intuitive, heuristic and impulsive, while System 2 is conscious, slow, controlled, analytic, reflective and systematic[10]. System 1 works well most of the time, but it has biases that it is prone to make, such as answering easier questions, ignoring statistics, anchoring and overconfidence. System 1 continuously provides suggestions to System 2 in the form of impressions, intuitions, intentions and feelings. System 2 is generally lazy and runs in a comfortable low-effort mode. Consequently System 2 often endorses or rationalises System 1's suggestion, turning impressions and intuitions into beliefs and impulses into actions[8]. The law of least energy applies here; to save energy and brain capacity the brain applies routines to our reasoning, operated by System 1. System 1 provides a mental model that represents the most probable state of affairs given past experience and current understanding[11]. System 2 can actively intervene in our thinking and mental model, and hereby limit the biases of System 1. How much and how well System 2 intervenes, depends on personal motivation, task instructions, cognitive capacity and time pressure, among others. In addition, people are prone to satisfice, to hold on to mental models that are good enough and thus saving themselves any additional cognitive effort[6].

This theory of two systems provides a good explanation of how people think, and thus how they think about the future. People consider a future that fits their current mental model. They confine themselves to this model until they find a good reason to give it up. Increased intervention by System 2 may result in modification or replacement of the routine mental model. Foresight studies can actively encourage System 2 thinking, hereby limiting routine thinking, biases and heuristics. This can result in an updated mental model that serves as a new reference point for decision-making and thinking about the future[11].

1.4. The value and limitations of foresight

Foresight studies create value by assisting in the creation and diffusion of knowledge across individuals and organisations[19]. More knowledge on future possibilities can result in increased risk awareness and contingency planning, the detection of weak signals of change and potential disruptions, and a better overall preparedness about the future. In addition, foresight studies are a tool for stimulating interactions between different stakeholders, hereby assisting in the strengthening of existing networks or the creation of new ones. These interactions can result in increased trust, communication and knowledge flow between different actors. Collective learning and knowledge creation reduces geographical, institutional or disciplinary boundaries between stakeholders and supports the formation of shared visions[19].

Foresight studies create cognitive value by updating or changing the mental models of individuals and organisations. Mental models are based on routines, past experiences, beliefs, norms, values and biases (see text box 2). However, the future is not an extension of the past and especially in science and technology, developments are often non-linear, disruptive and unpredictable. By actively engaging in foresight studies, mental models are challenged and updated with new information, hereby preventing tunnel vision and reducing the likelihood of biases based on routines and past experiences[6, 10-11]. In this manner, foresight studies can support double loop learning in which actors reflect on and adjust underlying assumptions, knowledge and norms[41-43]. In addition, foresight studies can create a mind-set or attitude for thinking out of the box and assist in exploring and dealing with cognitive, normative and social uncertainties[41].

Foresight studies can also create value for policymakers by detecting potential obstacles, and setting agendas and priorities. Furthermore, these kinds of studies have the potential to intensify public debate, increase the dialogue with society and muster public support[19]. A foresight study can provide information to policymakers on what the problem could be, what the policymaker's role might be in solving it, what norms and values may be challenged, who is involved and which future problems or opportunities could be faced[41 (p.110)]. All of this can result in better-informed policymaking. To recap, foresight studies are a tool to share and improve knowledge, create networks, change mental models, increase risk awareness and preparedness, recognise uncertainties, drive change and take an active role in shaping the future.

In addition to its values, there are also limitations to foresight studies. Foresight studies cannot predict the future and it should be made clear that they do not attempt to do so. Moreover, foresight studies do not limit or solve the uncertainties that are inherent to the future. Rather, they are concerned with anticipating possible futures and can provide handholds on how to deal with them[44]. Furthermore, foresight studies cannot be expected to lead to universal consensus, and are therefore not a "quick fix" for multisided policy issues[45]. However, these kinds of studies can assist in mapping different opinions, norms and values and create a better understanding among the actors involved.

A shortcoming of foresight studies is that their impact on decision-making is difficult to observe and measure. Foresight studies can lead to (over)optimistic expectation about the future, which could result in disappointment at a later stage. It is important to remain critical during the foresight study to ward against these and other unwanted biases. To increase the credibility of foresight studies it is recommended to include a fact-based foundation using analytical and exploratory scientific methods supplementing the often-used participatory and creative methods[46].

2. RIVM policy in relation to foresight studies

2.1. Moving to the centre of society with foresight studies

RIVM has no specific policy or strategy on foresight studies. However, general corporate strategy and policy, described in the *strategic programme 2015-2018*[47] and the *Routekaart RIVM 2020*[48], can be analysed to determine the RIVM's viewpoints and how these relate with respect to foresight studies. RIVM sees itself as the trustworthy advisor that aids both the government and society in striving for a healthier population in a healthier environment. According to the *Routekaart RIVM 2020*[48], RIVM has to anticipate, know and respond to what is happening in society. Therefore, RIVM tries to move from its current position at the side-lines to a position more in the centre of society. Establishing a better connection with society and its citizens is deemed essential to get the most out of the RIVM's expert knowledge. The RIVM tries to establish a more direct dialogue with society, for example via the Grenelle Dialogue programme on nanotechnology, which aims to map the views and interests of the different societal actors and stakeholders through a dialogue, without polarizing the debate. Foresight studies are an excellent way to encourage participation and interaction between experts, stakeholders and citizens, hereby moving to the centre of society.

2.2. Value changes and actions related to foresight

Expertise, reliability and impartiality are named as the RIVM's core values. There is great emphasis on the RIVM's (scientific) independence and impartiality. This need to stay independent is strongly felt by the employees and therefore there is a certain amount of restraint towards a more active role in society and increasing interactions with societal partners and citizens. A result of this strong focus on maintaining independence is that the RIVM provides facts, but regularly refrains from giving an opinion or interpretation of what is best to do, based on these facts. Making judgements, developing policy and setting priorities are often left to the policymakers. Citizens participating in the Grenelle Dialogue programme on nanotechnology said that the RIVM should show more courage and take a stronger stance on certain issues[49]. This corresponds with the RIVM's intended strategy change "van lief naar lef" (literally translated "from friendly to daring"). The RIVM aims to become more goal-oriented, vigilant and proactive, among other value changes[48].

The RIVM has determined 28 lines of action in the *Routekaart RIVM 2020*[48]. The nine lines of action related to foresight studies are:

- Choosing position in the centre of society
- Embedding social sciences in the RIVM
- Making contact with citizens (for example via panels and social media)
- Engaging in societal dialogues (for example on nanotechnology)
- Capture and secure relations
- Make employees aware of and stimulate their ability to learn
- Guide innovative processes
- Stimulate internal and external multidisciplinary collaborations
- Appoint top priorities in consultation with RIVM clients

RIVM has also specified ten priorities on which the organisation should strengthen their international position. Two of these are related to foresight studies:

- Health and healthcare systems, monitoring, foresight and the development of indicators;
- Risks of new technologies, with a focus on nanotechnology.

2.3. Innovation is encouraged to create a proactive attitude

RIVM places innovation high on the agenda by starting pilot projects and consulting with clients on new themes, products, techniques and methods. To encourage this, RIVM aims to create a safe learning environment and provides its employees the freedom to take more risks than usual. According to the *Routekaart RIVM 2020*[48]*,* innovation means anticipating changes in society and initiating innovation yourself. This refers to another change of attitude that the RIVM aims to accomplish: from reactive to proactive. Changing towards a more proactive attitude remains difficult in such a large and academic organisation. As mentioned above, foresight studies can play a role in this process by facilitating learning and innovation, and anticipating changes in society.

3. Analysis of foresight studies at the Centre for Health Protection and the RIVM

3.1. Technological and non-technological foresight studies

RIVM conducts foresight studies on both technological and non-technological topics. These studies range from smaller technology scanning exercises[50] to large normative scenario studies[29]. At least 13 foresight studies have been conducted or are ongoing in the period 2014-2015 (see Table 2 and appendix 2). These studies are performed at eight different departments across four centres[D]. GZB has recently finished two foresight studies and has two on-going projects, all of which are on technological subjects. The Centres for Safety of Substances and Products, and Sustainability, Environment and Health also conduct foresight projects mainly on technological subjects. This is in contrast with the Centre of Health and Society, of which all three foresight studies have a non-technological, more societal subject. The major sponsors or clients are the Ministry of Health, Welfare and Sport, and the Ministry of Infrastructure and the Environment. Other government departments, government agencies and the RIVM itself occasionally act as a sponsoring party.

3.2. RIVM uses a variety of foresight methods

The methods that can be used in foresight studies are diverse, as described in chapter 1.3. Analysis of 11 of the abovementioned 13 RIVM foresight studies (2 studies are in preparation) shows that during the period 2014-2015 the RIVM used 16 different methods at varying frequencies (see Figure 2A). Literature study (the reviewing of scientific and/or grey literature) is most often used. The frequency is similar when compared to other foresight studies in the Netherlands[28]. Information from literature is often used to determine the status quo and as input for other methods. In addition, this method can serve as a way to gather the views of scientists and other professionals about the future of a given subject.

Databases are also frequently used in RIVM foresight studies. Examples are databases for clinical trials, or certain products, and registers for population size, mortality or diseases burden. These data can be used directly or as input in quantitative methods, such as trend extrapolation and modelling, in which the RIVM has a strong background. For example in the recent *Public Health Status and Foresight Report 2014*[29] databases, trend extrapolation and modelling had a prominent role, as they were used to estimate future life expectancy and chronic disease burden, and to create 'business as usual' scenarios of the future.

Experts are regularly consulted in RIVM foresight studies, mostly via interviews and surveys. Due to the RIVM's network and reputation, experts in academia and related institutions are relatively easily accessible. Experts in business are sometimes more difficult to reach as the RIVM keeps some distance from companies to maintain its independence. This can vary depending on the subject and the department's network. Panels of experts were only used in one of the 11 RIVM studies. In contrast, European and Dutch foresight studies use expert panels in 50% of studies[28]. This difference

[D] The RIVM is organised in three domains (Infectious Disease Control, Environment and Safety, Public Health and Health Services) consisting of 12 centres containing a variable number of departments. Additionally, there are a number of supportive and managerial departments (http://rivm.nl/en/RIVM/Organisation).

might be explained by the fact that many, especially technological, RIVM foresight studies are conducted within a relatively short timeframe and have limited resources to appoint a panel of experts.

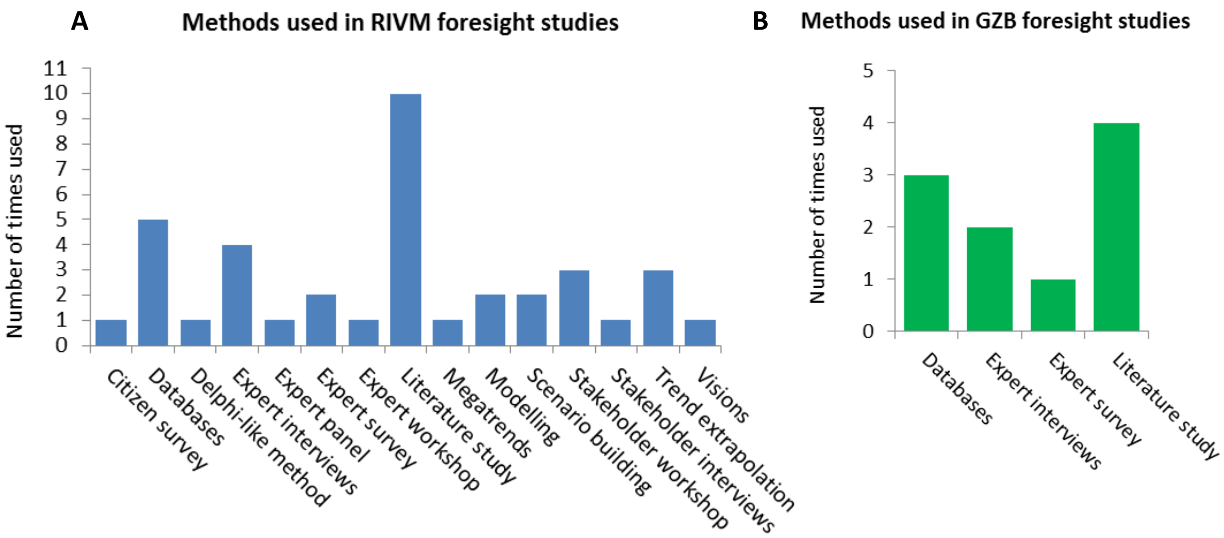

Figure 2. Methods used in GZB and RIVM foresight studies. A) Methods used in RIVM foresight studies during the period 2014-2015, including GZB (n=11). B) Methods used in GZB foresight studies during the same period (n=4).

Scenario-associated methods are not regularly used in recent RIVM foresight studies. This is in contrast with European and Dutch foresight studies in general, where they are applied in 42% and 50% of the studies, respectively[28]. It should be noted that about half of the European and Dutch foresight studies investigated in that report are performed in the field of social sciences, with a Dutch focus on policy and political science, human society, education and economics. This is different from the RIVM's fields of health and the environment, which could explain the finding that scenario-associated methods are not used frequently. Recently, RIVM has used normative scenarios in the *Public Health Status and Foresight Report 2014*[29] on the future of the Dutch healthcare system. As RIVM is currently developing this expertise, it might be expected that in the future scenario methods will be used in other RIVM foresight studies. This method would fit well with the RIVM's aim of positioning itself more in the centre of society, as societal norms, values, barriers and drivers are often included in these kinds of scenarios.

3.3. GZB only uses evidence- and expertise-based foresight methods

In their recent foresight studies GZB has used methods based on evidence and expertise (see figure 2B). The literature study and databases are descriptive, exploratory, and largely evidence-based methods that are particularly useful in the first, diagnostic phase of a foresight study. A literature study can also be non-evidence based when expert opinions about the future are extracted from scientific and grey literature. The expert interviews and surveys are based on expert opinions. All of the methods used by GZB are open and exploratory, although interviews can have a normative character. Evidence-based methods such as trend extrapolation and modelling are not employed by

Table 2. Overview of RIVM foresight studies 2014-2015

Project	Centre	Department	Sponsor	Status
Capacity building Foodture (Foresight in Food)	Health and Society	Foresight in Public Health	RIVM	Ongoing
Public Health Status and Foresight Report 2014[51]	Health and Society	Foresight in Public Health	Ministry of Health, Welfare and Sport	Finished
Sport Foresight study	Health and Society	Foresight in Public Health	Ministry of Health, Welfare and Sport	Preparation
Nanomedical devices - A horizon scan	Health Protection	Product safety	Ministry of Health, Welfare and Sport; Dutch Health Care Inspectorate	Ongoing
Nanomedicinal products[52]	Health Protection	Product safety	Ministry of Health, Welfare and Sport	Finished
New medical technologies[53]	Health Protection	Product safety	Dutch Health Care Inspectorate	Finished
Personalised medicine	Health Protection	Effects on Public Health	Ministry of Health, Welfare and Sport	Ongoing
Nanomedicinal products - A horizon scan	Safety of Substances and Products	Consumers and Product safety	Ministry of Health, Welfare and Sport	Ongoing
Synthetic Biology	Safety of Substances and Products	Gene Technology and Biological Safety	Ministry of Infrastructure and the Environment	Preparation
3D printing[50]	Sustainability, Environment and Health	Environment quality and Health	RIVM	Finished
Demand coverage Dutch drinking water supply 2015-2040[54]	Sustainability, Environment and Health	Sustainability, Drinking Water and Soil	Ministry of Infrastructure and the Environment	Finished
Prospective study demand for drinking water 2040 and availability resources[55]	Sustainability, Environment and Health	Sustainability, Drinking Water and Soil	Ministry of Infrastructure and the Environment	Finished
Technology Exploration National Security[56]	Sustainability, Environment and Health	Integrated Spatial Issues	Ministry of Safety and Justice	Finished

GZB, although they are used in foresight studies from other centres. Not using these methods has been a correct choice of GZB, as their recent foresight studies have all been on technological subjects. Using historical data to forecast trends is often not reliable in dynamic and unpredictable technological fields.

However, GZB does not use creative and interactive methods in their recent foresight studies, such as stakeholder and expert workshops, scenario's, and visioning workshops. As a result, GZB is not using a balanced mix of methods in their foresight studies. Creative and interactive methods are used in other foresight studies across the RIVM (see figure 2A and B). These kinds of methods can complement the already used evidence and expert methods by covering their weaknesses, such as a lack of learning potential and a difficulty in changing mental models. In addition, the interactive methods fit well with the RIVM strategy of moving to the centre of society as they allow for direct interaction and cooperation with groups of societal actors.

3.4. GZB foresight studies compared to RIVM corporate policy

A main aspect of RIVM corporate strategy is moving from the side-lines to the centre of society. However, this is not reflected in recent GZB foresight studies, as the used expertise- and evidence-based foresight methods are performed behind a desk without reaching out to citizens, stakeholders and society as a whole. By also using creative and especially, interactive methods, GZB foresight studies can connect to society and also contribute to the desired attitude change from reactive to proactive. GZB already uses these kinds of methods in other project, but not yet in their foresight studies. Knowledge on using creative and interactive methods specifically in foresight studies is present at other RIVM centres.

The *Routekaart RIVM 2020*[48] states 9 lines of action related to foresight studies (see chapter 2.2). GZB can improve on several of these lines of action by incorporating interactive and creative approaches in their foresight studies, as a result increasing the diversity of methods used. These lines of action are making contact with citizens, engaging in societal dialogue, capturing and securing relations, stimulating employees to learn through foresight and update their mental models, and stimulating internal and external multidisciplinary collaborations.

What does fit with RIVM corporate strategy is GZB's focus on science- and technology-related subjects. All four recent foresight studies are on technological subjects related to healthcare. Identifying the risks of new technologies is a RIVM priority as stated in the *RIVM Routekaart 2020*[48]. Furthermore, the Integrated Risk Assessment theme from the *RIVM strategic programme 2015-2018*[47] refers to the "early assessment of risks and benefits of new technologies" as a possible research topic to receive internal funding.

A possible explanation for the difference between GZB foresight studies and the RIVM corporate strategy could be a lack of time, funding, experience and other resources at GZB. GZB conducts mostly smaller technological foresight studies with teams of 3-5 people and a limited budget. Choosing the abovementioned methods (literature study, databases, expert interviews, and expert surveys, see paragraph 3.3) is an obvious choice. In addition, these are methods that staff members feel comfortable about and have experience with due to their mostly scientific backgrounds.

Another explanation can be the wishes of the sponsoring party. The sponsor has certain questions they like to have answered. It is possible that the sponsor does not see the benefits of including alternative objectives or using interactive and creative methods, but wants to focus on technological risks and opportunities. However, GZB, RIVM and its sponsors should try to avoid the pitfall of technological determinism. Technological developments are not the futures sole determinant. Social discontinuity should not be disregarded[41]. Especially with new science and technological developments, society should be involved directly from the early stages[57]. Interactive methods are an excellent tool to accomplish this.

4. RIVM foresight structure: weaknesses and opportunities

4.1. No overarching foresight structure

In addition to improving foresight studies, the RIVM can also improve on several organisational weaknesses related to foresight studies (see figure 4). As there is no overarching RIVM foresight structure it is difficult to find other foresight practitioners and know who performs which foresight studies at which department or centre. This results in restricted cooperation and limited knowledge transfer between departments and centres, a general issue at the RIVM[48]. A questionnaire confirms this image (see appendix 1). Around half of the questionnaire participants disagree with the statements that foresight practitioners are easy to find within the RIVM and knowledge on foresight studies is shared. As a consequence many foresight practitioners are on their own isolated island and have to reinvent the wheel when performing a foresight study. Improving this inefficient process can contribute to the overall quality of RIVM foresight studies. It should be noted that not all foresight practitioners are difficult to find. The *Public Health Status and Foresight Report*[29] study is conducted by the department of Foresight in Public Health and is well known throughout RIVM.

Figure 4. No overarching RIVM foresight structure leads to several organisational weaknesses.

4.2. High concentration of in-house experts

In addition to its weaknesses, RIVM also has several considerable strengths that can be used to seize opportunities and ward off threats (see table 3 for a SWOT analysis). The main strength of the RIVM is their high number and concentration of in-house experts on a wide variety of both health- and environment-related topics. In addition, certain departments have participated in larger foresight studies, such as the *Public Health Status and Foresight Report*[29] published every four years. The knowledge from these large foresight studies does not diffuse through the organisation and can therefore not benefit the smaller foresight studies. RIVM tries to address their reactive attitude and limited interaction with society via a policy shift as described in the *Routekaart 2020*[48]. Currently, these weaknesses are still present, although improvements are being made. It is hard to judge if, and how fast, these weaknesses will diminish over the coming years.

4.3. Seizing opportunities through foresight studies

There are several opportunities for the RIVM that can be seized through foresight studies. Foresight studies, combined with monitoring activities, assist in the earlier detection of new and emerging signals. In addition, they allow for directly connecting with society and thereby assessing the societal values regarding certain issues. An increase in foresight expertise, combined with the increased network formation that often accompanies foresight studies, can result in more assignments from external clients.

The RIVM should watch out for a loss of reputation if they are not able to anticipate changes in technology and society, but are instead surprised by new developments or undetected societal value shifts. In addition, this could lead to a detachment from society and as a result, an inability to adequately answer questions from government and other clients.

Table 3. SWOT analysis on foresight studies at the RIVM

	Strengths	**Weaknesses**
Internal	**1. Expert knowledge on diverse (technological) subjects regarding health and the environment** **2. Certain departments have experience with large foresight studies** 3. High knowledge on risks and risk assessment 4. Strong network and reputation both national and international 5. Library department with expert knowledge on literature databases and modest use of bibliometrics 6. Trustworthy advisor and independent position 7. Combination of desk & laboratory research	**1. Restricted cooperation and knowledge transfer between RIVM departments and centres on foresight studies** **2. No overarching foresight structure** 3. Still mostly reactive towards new technological and societal developments 4. Not a strong interaction with society, institute is positioned on the side-lines instead of the centre of society 5. Limited resources to address all new (technological) signals via foresight studies 6. Limited use of and experience with big data, scientometrics and text mining
	Opportunities	**Threats**
External	**1. Earlier detection of new and emerging signals from technology and society** **2. Connecting with society through foresight studies** **3. New external clients through network formation and generation of foresight expertise** 4. Increasing and strengthening network with different types of stakeholders 5. Increase knowledge on foresight studies to become (inter)national authority	**1. Inability to adequately answer questions from Ministries and other public organisations regarding new technologies and their potential impact** **2. Loss of reputation due to inability to anticipate new (technological) developments or societal trends** 3. Decrease in external assignments due to suboptimal expertise in foresight studies 4. New opportunities create new competitors 5. (Governmental) budget cuts make it difficult to conduct foresight studies 6. Lack of external support for conducting foresight studies and their added value

Sources: Employee interviews, RIVM report SWOT netwerken RIVM 2013[58], author's views

5. Recommendations

5.1. GZB should use interactive foresight methods

GZB should use additional kinds of foresight methods to improve their foresight studies and better connect with society. Recent GZB foresight studies use evidence- and expert-based methods, but do not incorporate creative and interactive methods. GZB is advised to use more creative and interactive methods to gain a more balanced method mix. In addition, especially interactive methods are an excellent tool to connect to society, promote internal and external cooperation, update mental models, and create a proactive and learning environment to provide the government with better anticipatory advice.

To use interactive methods in their foresight studies, GZB can build on the experience they gained from using these kinds of methods in other types of projects. Furthermore, they can cooperate with other centres and departments within the RIVM, as these groups have experience with using both creative and interactive methods in their foresight studies. This indicates the importance of a RIVM broad network of foresight practitioners (discussed below in paragraph 5.2) to increase knowledge flow and learning across departmental boundaries.

Interactive methods can also help in avoiding the foresight study pitfall of technological determinism. Technology is not the sole determinant of the future. It is the interaction of society with a technology that will eventually determine if and how a technology will be used[41]. Therefore studying societal norms and values regarding new technological developments is important. An example of a technology foresight study which did not only focus on the technological aspects, is the RIVM study on 3D printing[50]. This study mapped the guiding visions of producers and different user types of 3D printing via interviews and an interactive workshop. By assessing which normative wishes and visions influenced development, they gained a better understanding of the potential future direction of 3D printing. As a side effect, the interactive workshops resulted in a better overview of the different actors and their interests, and created an informal network on 3D printing for all actors involved.

If GZB does not use creative and, especially, interactive methods in their foresight studies they have a higher chance of missing societal signals and developments which might be of importance to the RIVM and the Dutch government. As a result, GZB will remain reactive to technological and societal developments, and will not be able to provide the Dutch government with proactive, anticipatory advice.

The choice of methods depends on the objectives of the foresight study, among other factors. As the objectives of RIVM foresight studies often depend on the sponsor’s wishes it can be difficult to incorporate more interactive and creative methods. For GZB to use more interactive and creative methods they will have to convince the sponsor of their importance related to RIVM policy and their added value to individual and organisational learning, network formation, and better insight in the societal forces shaping future (technological) developments, resulting in improved anticipatory advise for the client. In the end, the chosen methods should align with the foresight study itself. Using interactive or creative methods just for the sake of including them is not recommended

5.2. Create an internal knowledge network

The RIVM should aim to promote foresight knowledge diffusion and interdepartmental collaboration by creating an internal knowledge network. An internal network allows foresight practitioners to find and connect with each other, share experiences and problems, and gain advice. In addition, a network allows for the capture of new "ownerless" signals and assists in creating a proactive foresight culture. The intended increase in knowledge diffusion and collaboration will result in improved individual and organisational learning[59]. This might lead to more efficient and higher quality foresight studies, improved foresight expertise, a strengthened reputation, and possibly more external assignments (see figure 5 for an overview of recommendations to the RIVM as a whole and their intended effects). The creation of an internal knowledge network can count on the support of the upper management and, as shown by the questionnaire results (see appendix 1), the RIVM foresight practitioners.

The first thing the RIVM should do is organise a meeting for all RIVM foresight practitioners to discuss the start of an internal network. By actively engaging the intended users and asking how they want to shape the network, commitment to maintaining the network is increased. The following two actions are recommended:

1) Appoint a network chairman/chairwoman and/or secretary:
   The tasks of the chairman/chairwoman would be to maintain the network and the LINK community (see below), act as organiser for subsequent meetings, act as contact person within the network, keep up to date with all running RIVM foresight studies, and act as an advisor or sparring partner for RIVM foresight studies when required. However, another experienced network member could also fill this last task. The hours spend by the chairman/chairwoman could be compensated via the Strategic Programme RIVM (SPR), which are RIVM funds available for research, innovation and knowledge development. The amount of hours available to the chairman/chairwoman will depend on the tasks and should be decided upon during the abovementioned meeting of RIVM practitioners in consultation with upper management.

2) Create a LINK community:
   The RIVM tries to promote interdepartmental collaboration via an online platform called 'LINK', which can be used to create communities and find specific employees. Such a LINK community would act as an excellent platform to gather the different foresight practitioners in one place and allow easy communication. Additionally, documents can be stored online within this community or as a general working document on the RIVM's servers. In this way, the RIVM can centrally store all finished foresight studies and related documents (e.g. evaluations, new project descriptions), allowing members easy access and keeping an overview of what has been done in the past. In the future these documents can be used for benchmarking purposes. Furthermore, the LINK community could function as a place to report new and emerging "ownerless" signals. A difficulty might be that RIVM employees have a love-hate relationship concerning LINK, resulting in some employees actively using the platform and others actively avoiding it.

The network's activities should involve the organisation of presentations on finished RIVM foresight studies for the practitioners within the foresight network. The active sharing of experiences will stimulate learning and make sure that foresight practitioners stay in touch. Once a foresight study has been finished and evaluated, the project leader presents its study design and findings to the network. In addition to the results, the project leader also presents the process behind the project, the dos and the don'ts. By doing this, knowledge and experiences are shared and foresight practitioners can actively interact, ask questions, and provide and receive feedback, with the goal of learning and improving RIVM foresight studies.

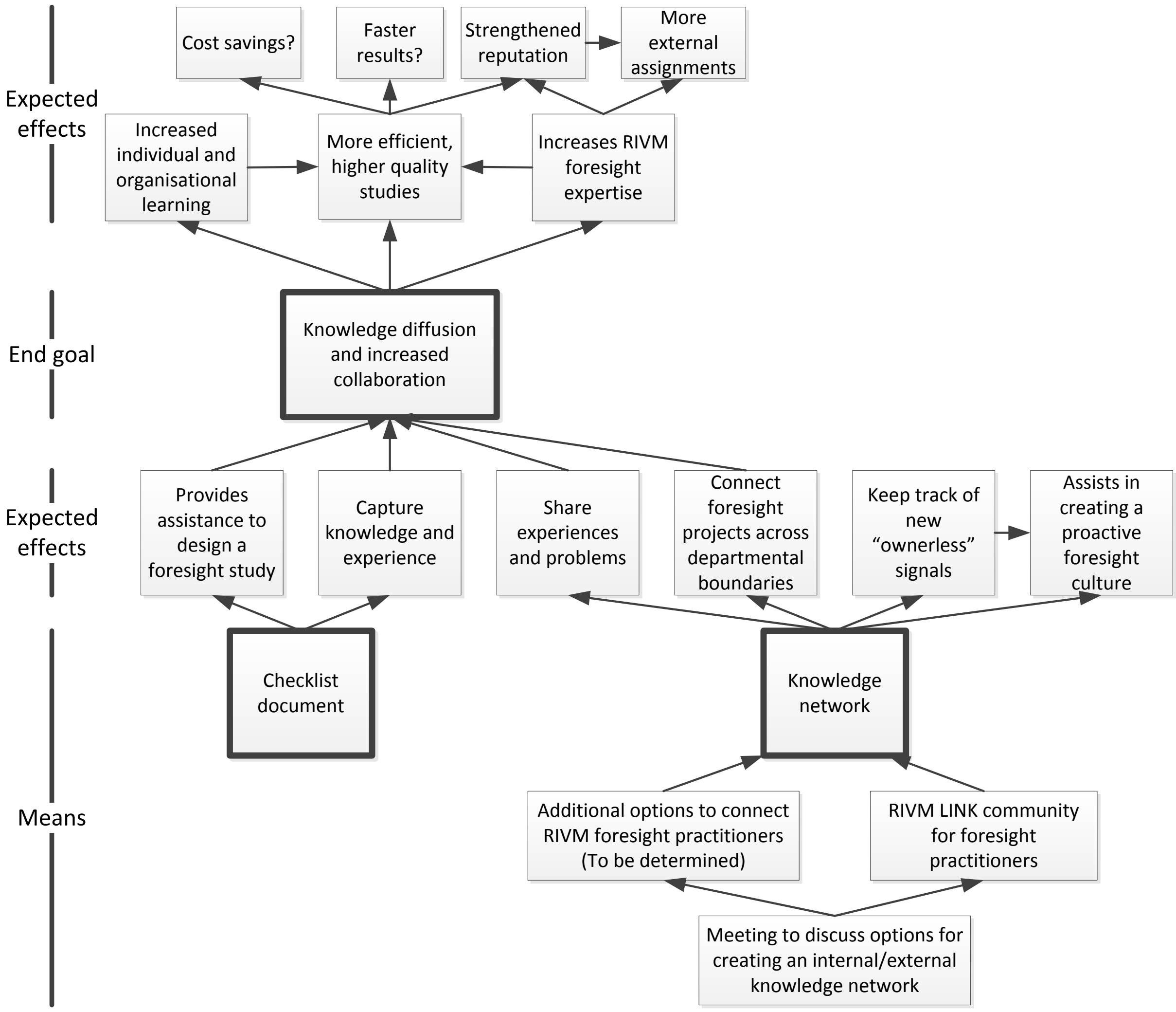

Figure 5. Recommendations to promote knowledge diffusion and increase internal collaboration. Drafting a checklist document and setting up an internal knowledge network of foresight practitioners will assist in RIVM-broad knowledge diffusion of foresight expertise and will assist practitioners with a structured approach to designing foresight studies.

The recommended network will only be a success if there is enough support and commitment from the RIVM foresight practitioners. In addition, an enthusiastic chairman/chairwoman that is willing to invest time and effort to run the network is crucial. Without both these factors the network will not be successful in increasing knowledge diffusion and learning across departmental boundaries. Currently, there is enough focal support for the network among RIVM foresight practitioners. However, it is uncertain if this support will remain when the network becomes a reality and the foresight practitioners have to start investing real time and effort. To increase the chances of continued support the foresight practitioners themselves should be given the freedom to determine the form and activities of the network, instead of implementing a required top-down structure. Furthermore, the function of chairman/chairwoman should be made more attractive by providing a limited number of billable hours, for example from the RIVM's SPR budget.

5.3. A checklist document and method selection tool for designing foresight studies

In addition to an internal knowledge network, the RIVM should draft a checklist document for designing foresight studies, combined with a tool for selecting methods. Such a checklist and method selection tool will support foresight practitioners in designing their foresight study. This would prevent groups from having to reinvent the wheel, hereby saving them time. Furthermore, such a document is a tool to capture knowledge and experiences, and make them explicit for other people to use (see figure 5). The questionnaire shows that a majority of foresight practitioners would have wanted a guideline document to help them design the foresight study. In addition, a questionnaire showed that almost all foresight practitioners think such a document would add to the quality of foresight studies within the RIVM (see appendix 1).

The checklist will focus on the design phase of a foresight study. In addition, the checklist will make sure that all relevant factors are taken into account before starting the foresight study. As a result, the quality of RIVM foresight studies is likely to increase. The checklist document and the method selection tool should be practical and easy to use. The guideline document might be particularly useful for less-experienced foresight practitioners conducting smaller foresight studies. Part 2 of this report describes the checklist document. In addition, a condensed working version of the checklist can be found in appendix 3.

5.4. Potential long-term options

Once the abovementioned recommendations are implemented the RIVM could go one step further by incorporating close national partners into the foresight practitioner network, such as the Netherlands Environmental Assessment Agency (PBL), the Rathenau Institute and the Health Council of the Netherlands. By incorporating other organisations that perform foresight studies knowledge can flow from the RIVM to other organisations and vice versa. This would fit well with a current RIVM-project commissioned by the Ministry of Infrastructure and the Environment on proactive scanning and monitoring, which also aims to form a national network. Proactive scanning and monitoring is related to foresight studies and serves to gather societal signals on which a foresight study could be performed, among other things. A downside could be that a large multi-partner network decreases interaction between individual network members, while this interaction is the most important stimulator for learning and sharing of experiences. An option would be to only maintain the internal knowledge network and invite guest speakers from other organisations to present the findings and process behind their foresight studies.

Another potential future possibility is the development of a RIVM strategy on foresight studies. This strategy could be about what separates a RIVM foresight study from other foresight studies. This would entail a kind of product branding that could help the RIVM in distinguishing itself from other organisations. However, due to the diversity of subjects and methods a strategy that is too specific could become restrictive and results in a potential decrease in foresight quality. Therefore, the development of such a strategy should be carefully discussed within the internal foresight network.

Once the checklist document has been completed, it should be supplemented over time with information on finished RIVM foresight studies. This information should be short (1 A4) and include a short description of the study itself, the rationale behind method selection supplemented with a simple figure on the method framework, and the study evaluation containing positive and negative experiences. A standard format would make the process more efficient. Furthermore, a list of RIVM foresight practitioners and their experience with certain methods should be made.

5.5. Summary of recommendations

To improve the quality of foresight studies at GZB and the RIVM as a whole, the following actions are recommended:

1) Improve alignment of GZB foresight studies to the RIVM's general corporate policy by using more interactive methods to connect to society.

2) Start an internal network of foresight practitioners by organising an initial meeting. Subsequently appoint someone willing to pull the network as a chairperson, and create a LINK community.

3) Draft and use a checklist document and method selection tool for designing foresight studies.

Part 2 – A checklist document for designing foresight studies

One of the recommendations from Part 1 was to develop a checklist document and a method selection tool to assist RIVM foresight practitioners in designing foresight studies.

6. A checklist document for conducting foresight studies

6.1. Rationale

RIVM foresight studies are performed on departmental islands, cut-off from the input and experience of other foresight practitioners. As a result, each project team has to reinvent the wheel and design their foresight study by themselves. A checklist document and method selection tool can assist foresight practitioners in this process. Furthermore, such a document is a tool to capture knowledge and experiences, and make them explicit for other people to use. A questionnaire among RIVM foresight practitioners shows that a majority would have wanted such a checklist document to help them design the foresight study. In addition, almost all foresight practitioners think that such a document would add to the quality of foresight studies within the RIVM (see appendix 1).

6.2. Goal

The goal of the checklist document is to assist RIVM foresight practitioners in designing their foresight studies. The checklist document will make sure that essential steps are not forgotten and decisions are made explicit. Furthermore, the document forces the foresight practitioner to consider and answer several important questions related to their foresight study. The foresight practitioner uses the outcomes from this checklist to select appropriate methods in an Excel-tool (discussed below), and build a method framework to conduct the foresight study.

6.3. Target audience

The target audience are foresight practitioners at the RIVM. This document can assist in the design of any foresight study conducted at the RIVM, no matter the subject or scope. However, the checklist and Excel-tool are likely to be most useful for smaller foresight studies performed by an inexperienced practitioner. Still, larger studies and experienced practitioners can benefit from this checklist and gather inspiration for new methods. In addition, non-foresight studies, such as scanning and monitoring projects, can also take advantage of the checklist and Excel-tool.

6.4. Checklist outline

Foresight studies consist of different phases, namely a preparation phase, execution phase and finalisation phase[2, 5] (see figure 6). The checklist document focuses on the preparation phase, which handles the design of the foresight study. This is the phase where decisions are made on how to conduct the foresight study. The checklist document is not a guideline that makes choices for you, but forces you to make choices yourself. The document covers the design of a foresight study from different angles, hereby making sure the project team considers and answers all relevant questions and does not skip important decisions.

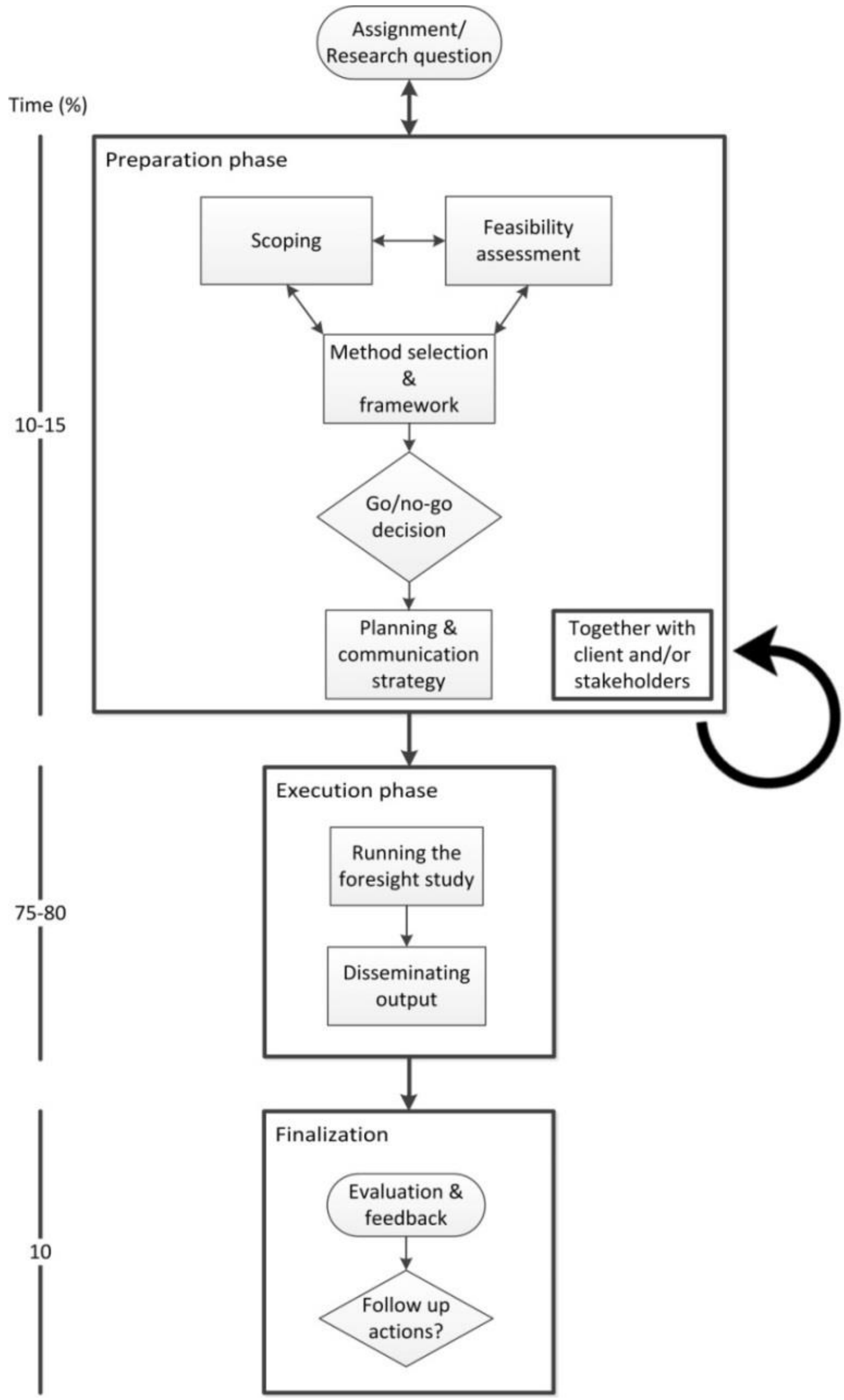

Figure 6. The different phases of a foresight study. An iterative process between the project team, client and key stakeholders with a focus on the interplay between feasibility assessment, scoping and method selection characterises the preparation phase. The resulting study proposal has to pass a go/no-go decision after which the foresight study is conducted. The execution phase takes most of the time. During finalisation the project team and client reflect on the study and decide on follow-up actions.

During the preparation phase the project team, in close collaboration with the client and/or key stakeholders, assesses study feasibility (chapter 7), determines the studies' scope (chapter 8), and selects methods to build a method framework (chapter 9). The developed Excel-tool assists in selecting methods. It contains a list of 63 methods used at varies points in a foresight project. These methods are scored on 18 characteristics (e.g. method type, costs, time). In addition, the Excel-tool provides information on advantages, disadvantages, additional reading, potential outputs, and general comments. The tool allows for the selection of methods based on preferred and required characteristics.

Feasibility, scoping and method selection are performed simultaneously and are characterised by interdependencies. For example, the scoping phase determines method selection, but the use of certain methods also has an effect on the studies' feasibility. As a result, choices have consequences for other parts of the foresight study. During this preparation phase, the structure of the foresight study is established, described and discussed with the directly involved parties. This initial phase is of great importance for the success of the foresight study. Therefore, decisions should be made carefully and in collaboration with the client(s) and/or key stakeholders. At the end of the preparation phase, the parties involved have to make a go/no-go decision to invest further resources and conduct the foresight study.

The document does not discuss the execution and finalization phases. Still, the Excel-tool does point to additional reading and/or guides for a number of methods. In addition, appendix 2 contains a list of recent RIVM foresight studies, foresight practitioners, and methods in which they have experience.

6.5. Sources

This checklist document is based on a literature study of several sources that focus on the project management of foresight studies. A number of large guidelines have been made over the years and this checklist document aims to capture the most significant steps in the design process of foresight studies by comparing the different references. The most important sources are the:

- European Foresight Platform (http://www.foresight-platform.eu/)[60]
- Foresight Methodologies Text Book - Training Module 2[44]
- FOR-LEARN Online Foresight Guide (http://forlearn.jrc.ec.europa.eu)[61]
- Integrating Foresight in Research and Investment Policy Formulation[2]
- Introduction to foresight and foresight processes in practice[5]
- Praktische handleiding voor regionale toekomstverkenning in Nederland[62]
- Uit zicht – toekomstverkennen met beleid[41]
- UNIDO Technology Foresight Manual Vol 1 – Organization and Methods[35]

A limitation is that some of the abovementioned sources are based on each other, therefore repeating the same information. Nonetheless, these sources are considered reliable, as they have been commissioned by reputable international organisations (e.g. United Nations, European Union) and drafted by experienced foresight practitioners.

To supplement the written sources, external consultation on the form and content of the checklist document took place with two external foresight experts, namely Ellen Willemse and

Patrick van der Duin. Ellen Willemse of the Netherlands Study Centre for Technology Trends (STT) has recent practical experience in performing foresight studies. Dr. P.A. van der Duin, assistant professor at the Delft University of Technology, is an expert on foresight methods, a board member of the Dutch Future Society, and has previously worked in the public sector as a futurist. In addition, several RIVM foresight practitioners, namely Cornelle Noorlander, Leendert Gooijer and Jeanne van Loon, were interviewed to gain input and feedback on the form and content of the checklist document.

The Excel-tool is based on both scientific and grey literature regarding foresight methods. This includes literature reviews on multiple methods and articles that cover specific methods in depth. Methods or method characteristics not discussed in literature were scored by the author through comparison with other, similar methods. Due to the flexibility of many methods and the author's own inexperience the Excel-tool is likely to contain a number of errors.

6.6. Future updates

There are several ways to improve the checklist document and the Excel-tool for method selection in the future:

- Add written evaluations from finished foresight studies. This transforms knowledge from tacit to explicit, so other foresight practitioners can easily access it and take advantage. The evaluation should be short (~1 A4) and contain a study description, the rationale behind method selection, a simple figure of the method framework, and a study evaluation containing positive and negative experiences. Designing a standard format would make the process more efficient.
- When a user uses this checklist document to design a foresight study, he or she should provide feedback on the strengths and weaknesses of this guideline so it can be improved for future use. Appointing a responsible person for maintaining this guideline is recommended.
- The list of RIVM foresight studies, practitioners, and used methods should be updated over time (see appendix 2 for a current list). Ideally, a responsible person is appointed from the recommended internal knowledge network of RIVM foresight practitioners.
- The Excel-tool should be kept up-to-date and expanded by RIVM foresight practitioners with information on costs, time, personnel usage, and updates in other characteristics. New and/or alternative methods should be added to the Excel-tool over time.

7. Feasibility assessment

7.1. Assessing feasibility through questions

The goal of assessing feasibility is to determine whether the foresight study can obtain satisfactory results given the study's context, before committing substantial resources. In addition, the feasibility assessment will provide information on which shape the foresight study must take to obtain the most valuable results. Furthermore, feasibility assessment forces you to make assumptions explicit and communicate with your client and/or key stakeholders.

Study feasibility is assessed via a number of questions and sub-questions. These questions force the foresight practitioner to think about the intended foresight study and surrounding forces. Answers to these questions will help to gain a clearer picture of the project itself, determine if the foresight study is necessary, if and how it adds value, what specific direction it should take and in which form it can have the most impact. In addition, it forces the foresight practitioner to reflect on possible obstacles and determine the project's position in the socio-economic landscape. Perhaps it is not (yet) possible to provide (complete) answers to all of these questions. Furthermore, some questions might not be applicable to the specific foresight study under consideration. After assessing feasibility, the project coordinator and the sponsor should decide whether to proceed, refocus, or cancel the foresight study. The following paragraphs introduce the questions in no particular order.

7.2. Why are we conducting a foresight study?

It is important to determine why you are conducting the foresight study, how it is different from already present exercises and how it will add extra value to the client and other stakeholders. Other actors have most likely performed a number of activities or foresight studies on your subject, and perhaps these activities already provide the answers the sponsor is looking for. Knowing what has been done can help to refocus the foresight study or can be used as input.

Q: Why are we conducting a foresight study?

- *What is the added value of the foresight study?*
- *Is the subject still relevant in the future?*
- *What activities or studies on the same subject are already done or on-going?*
  - *Can I make use of these studies?*
  - *How can I differentiate from these studies or add additional value?*

7.3. Clients, actors and stakeholders

Managing expectations is an important part of any project. High or unrealistic expectations can lead to dissatisfaction about the studies' results. Communicating with the client about his/her expectations during and after the study will help in getting everyone on level terms and give direction to the project. This includes a discussion on how the client will use and/or implement the results of the foresight study. Having discussions during the project with the client and/or other stakeholders on wishes, aims and expectations will make sure the foresight study remains on course.

Q: Who is the main client or sponsor of the foresight study?

- *What are the expectations of the client towards the foresight exercise?*
- *How will the client use the results of the foresight study?*

It is recommended to determine as many actors as possible related to the subject of the foresight study and chart their importance and relationships. Numerous tools are available to help in conducting an actor or stakeholder analysis and you can make the analysis as elaborate as is necessary for your project (tool example [63]). The actors can be departments, companies and organisations, but it is preferred to name specific persons, as these are the real actors. However, taking into account the organisational structures surrounding these persons is recommended as these structures will guide and frame their decisions and interactions[46].

When knowing the actors involved, one can assess if any of the actors is able to act on the results and therefore contribute to the potential success of the foresight study. These actors should be actively involved in the foresight study, either in the preparation or execution phase, to prevent one-way transmission of results. Building trust and mutual understanding ensures actor commitment towards the foresight study and its results. If there is no one to act on or use the results then why perform a foresight study? Even for unsolicited advice, there should be a willing acceptant. In addition, if the support for, or success of, the foresight study depends on only one actor the study could run into problems if this actor changes position. Knowledge on the actors, their importance and relationships will also help in answering the subsequent feasibility questions.

Some actors are important to have on board as they may help the exercise through their network, influence or ability to act. Other actors might act as ambassadors that give the study momentum and help to convey the studies' message. However, connecting big names to the foresight study could result in rivalries and misplaced expectations.

In addition to helpers, it is possible that some actors will oppose or hinder the foresight study. Perhaps the foresight study addresses questions that these actors see as their territory or they do not see the potential value of the foresight study. Try to reduce such threats by for example changing focus, starting a dialogue or actively involving them in the study.

Actors that are affected by the foresight study, either directly or indirectly, will most likely respond to the results when they are made public. Knowing who is affected and involving them in the study increases the likelihood of a positive reaction towards the results. In addition, affected parties should be considered as stakeholders and therefore their input might be of value.

Q: Who are the main actors related to the subject of the foresight study?

- *What position does each actor take?*
- *Are there key stakeholders that should be involved in the study?*
- *Which actors are under your control or influence, and which are not?*
- *Which actors can help the foresight study? Which actors might oppose it?*
- *Are there initiatives or agendas that could influence the foresight study, in scoping, need for timing or cooperation?*
- *Which of the actors is in a position to act on the result of the foresight study?*
- *Are there potential ambassadors and should they be approached?*
- *Is there enough support for the foresight study?*
- *Which actors might be (in)directly affected by the results of the foresight study?*

7.4. Study landscape

Foresight studies are always embedded in a wider political, economic, and cultural context. This context depends on the subject, but can have a large influence on the success, direction, and objectives of the foresight study, and should therefore be analysed beforehand. In a context marked by conflict between actors, one of the aims can be to map normative values, develop mutual understanding, and start a conversation. Oppositely, in areas of complacency one might try to introduce new perspectives and create a sense of urgency or crisis that demands immediate action[35].

Knowing what the attitude is towards foresight studies can help you determine which approach you should use. If there is no tradition of participatory approaches, using these kinds of techniques can make engaging stakeholders difficult. Furthermore, if the landscape is used to working with hard data it might be prudent to include some quantitative techniques into your method framework to win over these actors. If the involved actors have an innovative mind-set, it might be possible to try some uncommon methods. Discuss the methods you plan to use with the client and/or key stakeholders to increase credibility and ensure their support[32].

A controversial subject can have influence on the direction of the foresight study and its reception by the public. If there is no societal consensus on the subject, or if no consensus is expected in the future, assessing the normative and social uncertainties in addition to the cognitive uncertainties should be considered as an important study objective[41]. If a subject has had recent media coverage, the study and its results might attract more attention. This attention can be used for the good of the foresight study as it might motivate stakeholders to support the study. Thus, following the news on the subject of your study is advised.

Q: What kind of techno and socio-economic landscape surrounds the subject?

- *What are the current Political, Economic, Social, Technological, Environmental, Legal (PESTEL) factors surrounding the subject?*
- *Is the subject's landscape characterised by conflict or complacency?*
- *Is there a culture of collaboration?*
- *What is the general attitude of the landscape towards foresight studies?*
- *Is the subject of the foresight study potentially controversial?*
    - *How am I going to deal with a controversial subject?*

If the subject contains a strong political aspect, it is advised to think about the political context. Some technological foresight projects might not be directly political now, but politicians might use (public) results in the future, especially when these results come from the RIVM. Thus, thinking about the political position of the subject and its potential impact might be prudent.

If the foresight study aims to give policy advice or stimulate action by policymakers, the results have to be in harmony with the policy-making process in terms of timing, cultural compatibility and usability. By linking with already on-going activities or agendas, the foresight study gains in legitimacy. Involving important political decision-makers in the foresight study can help in making sure the results are acted upon. Working together will build mutual trust, but their participation should not jeopardise the studies' creativity and independence. There should be clear agreements on the role of the policymaker.

It is important to determine the position of the foresight study in the current policy cycle[E]. If new legislation or policy is being formed, a foresight study can have a direct impact on this process. Alternatively, if a subject is not yet on the policy agenda a foresight study can assist in getting it there. Furthermore, if certain actors ask parliamentary questions regarding the subject of the foresight study these actors might also act as ambassadors for the studies' results.

Q: What is the political context of the foresight study?

- *Who are the main political actors with regards to the subject?*
- *What is the political culture surrounding the subject?*
- *What is the position of the foresight study in the policy cycle?*
    - *Is the subject already on the policy agenda?*
- *Is the political environment stable or instable?*
- *Can the study link up with already on-going activities or agendas?*
- *Can policy-makers be directly involved in the design or execution of the foresight study?*
- *Is the foresight study aiming for a certain policy implementation?*
- *How will you generate policy support for the foresight study?*

7.5. Achievements, resources and evaluation

To keep the project specific it is important to state the results that the foresight study should achieve, and when you and the client will be satisfied with the results. Giving a timeframe for achieving these results provides focus and urgency to the study. These kinds of explicit matters will help in evaluating the foresight study afterwards. Thinking about how you are going to evaluate the study, and with whom, can help in designing and managing the project[27]. Considering if there are enough resources (time, money, people and competences) to finish the foresight study and gain useful results is critical, but often it is only possible to answer this question after the scoping, method selection and framework-building sub-phases are completed.

Q: What do you want to achieve with the foresight study?

- *When are you and the client satisfied with the results?*
- *What are the measureable outcomes?*
- *When do you achieve your results?*
- *How are you going to evaluate the foresight study?*
- *Are there enough resources to conduct the foresight study and gain valuable results?*
- *Are the necessary capabilities available to conduct the foresight study?*

7.6. Aligning with RIVM policy

As argued in Part 1 of this advice report, it is important to align the foresight study to RIVM corporate policy. Furthermore, there might be specific RIVM policies or strategies on the subject of the

[E] The policy cycle is a theoretical approach to analyze the policy process in a cyclical manner. It consists of different stages: agenda setting, policy formulation, decision-making, implementation and evaluation foresight study. By taking current policy into account, the study becomes more relevant for the RIVM.

Q: How do we align the study with RIVM policy?

- *Are there additional RIVM policies or strategies influencing this foresight study?*
- *How do we connect to society with this foresight study?*
- *How do we capture and secure relations?*
- *Are we going to collaborate with internal or external multidisciplinary parties?*
- *How are we going to be more proactive and show guts?*

8. Scoping a foresight study

8.1. Scoping involves three tasks

During the scoping phase, the project team, the client and/or relevant key stakeholders decide upon the different parameters that determine the form and scope of the foresight study. During the scoping phase, the parties involved review different foresight options, assess requirements against current capabilities and resources, and determine if the current organisational structures, routines or arrangements need to be adapted to conduct the desired study. The product of this phase will be a blueprint of the foresight study, also containing the desired methods and method framework (the scoping and method selection overlap). The scoping phase involves three tasks:

1) Gathering of background information into past and ongoing activities mostly through web searches (overlaps with the feasibility assessment).

2) Collect views and advice on the foresight study from other foresight practitioners, the target groups, different stakeholders, the client or sponsors via bilateral discussions. For large studies, consider organising scoping workshops. The aim is to gather ideas and obtain commitment of future support and participation. Early involvement in the foresight study results in stronger commitment of actors.

3) Design and present different foresight project options towards the client and possibly other stakeholders to receive feedback. Use the scoping parameters discussed below to generate a number of different project blueprints for further discussion. The parties involved decide upon one of these blueprints as a basis for the foresight study. However, it is important to stay flexible to changing conditions during the project.

8.2. Focus

Each foresight study has a certain focus, which can be on a specific issue (global warming, social inequality), on a geographical territory (international, European, national, regional, local), on a specific sector (public healthcare, automotive industry, nanomedical devices) or on a combination of these factors. Often the situation or the client predetermines the focus. However, it is worth spending some time together with the main stakeholders to define the focus more closely before starting the foresight study to help avoid misplaced expectations and streamline the study from the onset[64]. The foresight practitioner and the client should determine if the subject is appropriate for conducting a foresight study. In addition, the level of required focus or detail should be made explicit. The level of focus can be broad (e.g. Energy in Europe) or narrow (e.g. future solar panels in the Netherlands).

8.3. Perspectives and uncertainties

A foresight study can be approached from different perspectives and take into account different uncertainties. These perspectives and uncertainties influence the choice of methods and direction of the study. Therefore, several choices have to be made:

1) Stable vs. unstable. What can you expect of the future? Can you expect a stable, continuous future or is the future likely to be unpredictable and dynamic? Demographic patterns or life expectancy might fit the first category, while new technologies or complex and multi-interest subjects fit the latter. When expecting a continuous future one might rely more on quantitative methods such as trend extrapolation containing a margin of uncertainty. However, when the future is characterised by instability qualitative methods are more appropriate[41 (p.71)].

2) Kinds of perspective. What perspective should we adopt? A topic can be approached from a scientific, technological, institutional, social or economic perspective, among others. A mix is also appropriate to establish an integrated approach. The adopted perspective should match the chosen objectives and desired outcomes. The choice and design of methods is influences by the chosen perspective.

3) Types of uncertainty. What kinds of uncertainty do we focus on? Often, cognitive (knowledge) uncertainties are a major focus of foresight studies, while social and normative uncertainties are regularly ignored[41(p.74)]. In these studies, the future is assumed to be 'normatively neutral' and therefore 'objective' and devoid of statements about (un)desirability, values or political statements. Social and normative uncertainties can be restricted if one can assume there is, or will be, normative consensus about the subject. However, when consensus is not expected, normative and social uncertainties should play a prominent role in exploring the future. It is not always clear if one can assume social and normative consensus. Normative uncertainty should be explored when[41 (p.80)]:

   - multiple societal groups with very different values and interests are affected by the subject of the foresight study;
   - it is clear from the start that political parties will have different views on the matter;
   - actors with very different perspectives on a cultural, social, economic, religious, knowledge, or accountability level have to work together to decide the outcome of a process;
   - the subject concerns a controversial issue;
   - distribution of resources is scarce;

   Alternatively, it can be useful to assume normative consensus and only focus on cognitive uncertainties in the following circumstances[41 (p.81-81)]:

   - If the level of normative and social uncertainty is relatively small compared to the cognitive uncertainty;
   - When discussing normative uncertainties might distract from exploring the future or even paralyse the whole process due to strong opposing views;

- When stakeholders all support the same desirable future;
- When the relevant actors have a shared background, the same level of knowledge and a common purpose;
- When ignoring normative and social uncertainties is made explicit in the question. This might be the case when the foresight study will serve as input for a (political) decision process in which the normative and social uncertainties will be addressed.

4) Top-down vs. bottom-up. A top-down approach works according to a fixed procedure and usually involves groups of experts. Bottom-up approaches put more emphasis on interaction and the processes of information gathering, dissemination and result implementation are itself the subject of discussion[65].

5) Product vs. process. A product-oriented approach emphasises tangible outcomes (e.g. reports, action plans, scenarios, checklists), while process-oriented approaches focus on intangible outcomes such as network building, learning processes and creating a foresight culture and mind-set[65].

8.4. Target groups

Target groups consist of direct users and indirect users that are either interested in the results or affected by the foresight study. It is important to have an overview of the possible target groups, as some results will be appropriate for some groups and not for others. Gaining an understanding of potential users can help in designing a foresight study that maximises outcomes. The potential users depend on the subject of the study. The actor/stakeholder analysis performed during the feasibility phase can be of assistance. An overview of the target groups and involved actors will help in decision-making during the study. For example, when you need to select participants or stakeholders for a certain method you can use this overview to select actors from all relevant user groups.

8.5. Study objectives

A foresight study can have multiple main and side objectives, which fall within nine broad objective families (see Part 1, chapter 1.2 for families and topics). The objectives need to be carefully defined, clear and unambiguous from the start of the foresight study. The goal is to create a clear understanding of the objectives among the client, sponsors, project coordinator and the implementing staff. Therefore, they should be drawn up in close collaboration with the project team, the client and other important stakeholders. The objectives should be realistic in relation to the available money and time. If there are multiple objectives it should be clear on which emphasis is placed, as this will influence the choice of methods. Critical issues when defining the objectives[66]:

- Involve the client/sponsor
- Involve key stakeholders when applicable
- Be realistic (take into account time, money, personnel and capabilities)

- Make the objectives clear and easily understandable, as they will serve as reference point throughout the study and for evaluation.

8.6. Outputs

The broad objectives are translated into more specific outputs that the foresight study should produce. Desired outputs may vary among actors and therefore they should be discussed with the client and when applicable other relevant stakeholders. When defining outputs take into account that they fit the stakeholders' needs, the set objectives and the specific context, and that they are realistic. Defining all outputs is crucial, as they play a role in method selection. Outputs that are not stated beforehand will not be addressed adequately later on. However, do not mention anything that might be done, as the success of the foresight study will be measured against the achieved outputs[67].

Outputs can be either formal/tangible or informal/intangible. Formal outputs, such as reports, should be described in more detail by stating the topics, structure, length etc. Early templates can be used as a communication and discussion tool. The outputs are likely to address different audiences. Therefore, establishing which interested groups might benefit from the different outputs is useful. The table 4 provides some examples of different kinds of outputs.

Table 4. Examples of outputs

	Formal outputs	**Informal outputs**
Material for long-term reference and dissemination activities beyond those organisations directly involved in the foresight	Reports, books, databases, electronic records (videos, web resources).	Networking with foresight activities and actors in other settings, etc.
Dissemination within those organisations directly involved	Workshops, newsletters, press articles, websites.	Visions developed in workshops, results and evaluation circulating within networks.
Networking	Institutionalisation of networks e.g. through formation of permanent organisations and meeting places.	Development of new networks or new links established within existing ones.
Strategic process	Formal incorporation of results within strategic processes, e.g. through use of lists of key priorities as a framework for assessing projects and plans.	Informal incorporation of results and knowledge of networks and key sources of knowledge, within strategic processes.
Source[35]		

8.7. Time Horizon

For a foresight study, the time horizon should lie beyond the normal planning horizon of the actors involved[F]. Common sense and pragmatism should guide the selection of the time horizon. Take into account that different time horizons are suitable for different types of methods. The further away the time horizon, the less suitable predictive and quantitative methods become. The time horizon depends largely on the subject and the associated sector. Short 5-year time horizons might be suitable for dynamic and fast changing technological fields. In the public sector, it usually varies around 10 to 20 years, while for large infrastructure projects it might be closer to 30 to 50 years. Foresight studies with the objective to incite action tend to have a shorter time horizon to be able to influence today's decisions and prevent becoming irrelevant to current policy makers. Studies that focus on creating visions will have longer time horizons to take into account long term changes such as demography or global warming. Sometimes a variable time horizon can be chosen, to stimulate future thinking in general without fixing on a specific number[27]. When determining the time horizon one should take into account the schedule of decision-making and the degree of rigidity and motivation among actors[68].

8.8. Resources

When scoping a foresight study one should take into account the available resources including financial resources, time, (political) support, human resources and institutional resources[35]. The costs of a foresight study depend primarily on the duration, the amount of participants and the methods used. The shorter the study and the less people involved, the cheaper it will be. The financial resources can either be determined beforehand, resulting in the objectives, outputs and methods being adjusted to fit the available financial resources or it can be the other way around where the foresight study is scoped and financial resources are sought afterwards to cover the expected costs. Costs mostly result from[35, 69]:

- Running the project team;
- The choice of methods;
- Organisation of meetings and events, where possibly the travel costs of participants will be covered;
- Production and dissemination of publicity material and results;
- Subcontracting of certain work, such as extensive consultation processes involved in questionnaire surveys
- Other activities

The project team and the client should agree on the time available for the foresight study. The available time can be decided beforehand, whereupon objectives, outputs and methods have to fit within this timeframe. It can also be the other way around, placing emphasis on objectives, outputs and methods and adjusting the timeframe accordingly[70]. To gain better insight in the

[F] When designing a signalling or monitoring exercise, which are conducted at numerous RIVM departments, the time horizon becomes less important. However, when results from these exercises are used to think about, for example, future impact, the time horizon becomes relevant again.

available time and work a work-breakdown structure can be made where all aspects of the foresight study are broken down in sub-projects (for more information see https://www.workbreakdownstructure.com/nl/). The available time has a large impact on the number and choice of methods and the method framework. Foresight studies normally last between 6 months and 3 years. Foresight can also become a continuous activity, for example through periodically performed exercises or a continuous horizon scanning programme.

Support is an important resource as it creates momentum and enables action. Support has to come from within the own organisation, but can also come from outside (e.g. politicians). Knowing that an individual with authority supports the study can have a beneficial effect on the project team. Such a person can make his/her support clear by opening and attending workshops or other activities, or through active communication[35].

Human resources have an effect on costs and on the methods that can be performed. For conducting a successful foresight study one needs expertise in the subject area. In addition, certain foresight methods require experience and/or expertise. However, additional support can overcome a lack of experience and therefore people new to the field should not be discouraged. Different skills might be needed at different stages of the foresight study[71]

The RIVM has certain resources that can be of value during a foresight study. An example is the library department that can assist with literature searches, building a search strategy, provide daily news updates on almost any topic and help with basic bibliometrics exercises. Furthermore, the RIVM has a modelling department, which can assist in certain quantitative methods. The RIVM also has access to a number of non-public databases.

9. Method selection & framework

9.1. How to select foresight methods

Unfortunately, no simple guideline for selecting and combining methods exists, as many of the methods can be used in multiple ways and for multiple goals. Furthermore, the wide variety of subjects and study contexts complicates the options for general guidance[35]. The selection of methods depends upon the criteria determined during the feasibility assessment (chapter 7) and scoping (chapter 8) phases. The most important criteria are study objectives, available time, financial resources, desired outputs, prevalent uncertainties, and required method characteristics (described in chapter 1.3)[2, 35]. Other considerations could be the competences or experience available in the project team, and the suitability for combining with other methods, either for complementary results or as input for a subsequent method.

The goal is to select a balanced mix of methods to build a method framework that fits the purpose of the foresight study. Address potential pitfalls and risks in your design. Weaknesses of one method should be offset by another method. One way to cover weaknesses is by selecting a method from each corner of the Foresight Diamond (see figure 1, chapter 1.3). A foresight study often consists of an orientation or diagnosis phase, which is partly covered during feasibility assessment and scoping; a prognosis phase where forward-looking methods are employed; and a prescription phase where decisions and future actions are determined. Ultimately, consult with the client and/or key stakeholders on the selection of appropriate methods and the framework.

9.2. Excel-tool for method selection[G]

A developed Excel-tool allows for the selection of methods based on the decisions and considerations made during feasibility assessment and project scoping. Subsequently, these methods are used to construct a method framework (see 9.3). The Excel-tool describes 63 methods and tools that can play a role during the foresight study. Some of these methods help to prepare the study or orientate on the subject, some methods study the future, and others can be used for decision-making. The Excel-tool describes for each method the following characteristics:

- General description of the method
- Advantages
- Disadvantages
- Comments
- Potential output
- Objective families[28] (see chapter 1.2)
- Method families[32]
    - Creativity, Descriptive and matrices, Statistical, Expert opinion, Monitoring and intelligence, Modelling and simulation, Scenarios, Trend analyses, valuing/decision/economic
- Method characteristics[36]

[G] The tool is not included in this report, but is available as a separate Microsoft Excel file. If interested please contact the author (r.vd.stijl@gmail.com), or the RIVM supervisors Dr. Ir. Connie Brouwer (connie.brouwer@rivm.nl) or Ir. Robert Geertsma (robert.geertsma@rivm.nl).

    - Creativity, interaction, evidence, expertise, (see chapter 1.3)
    - Predictive, exploratory or normative
- Method function
    - Diagnosis, prognosis, prescription
- Kind of data
    - Quantitative, semi-quantitative, qualitative
- Suitability for visualisation of results
- Suitability for combining with other methods
- Method useful in uncertain environment
- Method useful in complex environment
- Level of interaction between participants
- Level of experience/skill needed to perform the method
- Experience available at the RIVM
- Recommended time horizon
- Costs
- Time in months
- Personnel usage
- Recommended additional reading

The Excel-tool can filter methods based on the abovementioned characteristics. In the Excel-tool, the filter is shown as a small arrow in the lower right corner of the title cell of each filterable characteristic. Click on the arrow and select the input for that specific characteristic to filter the methods (see figure 7).

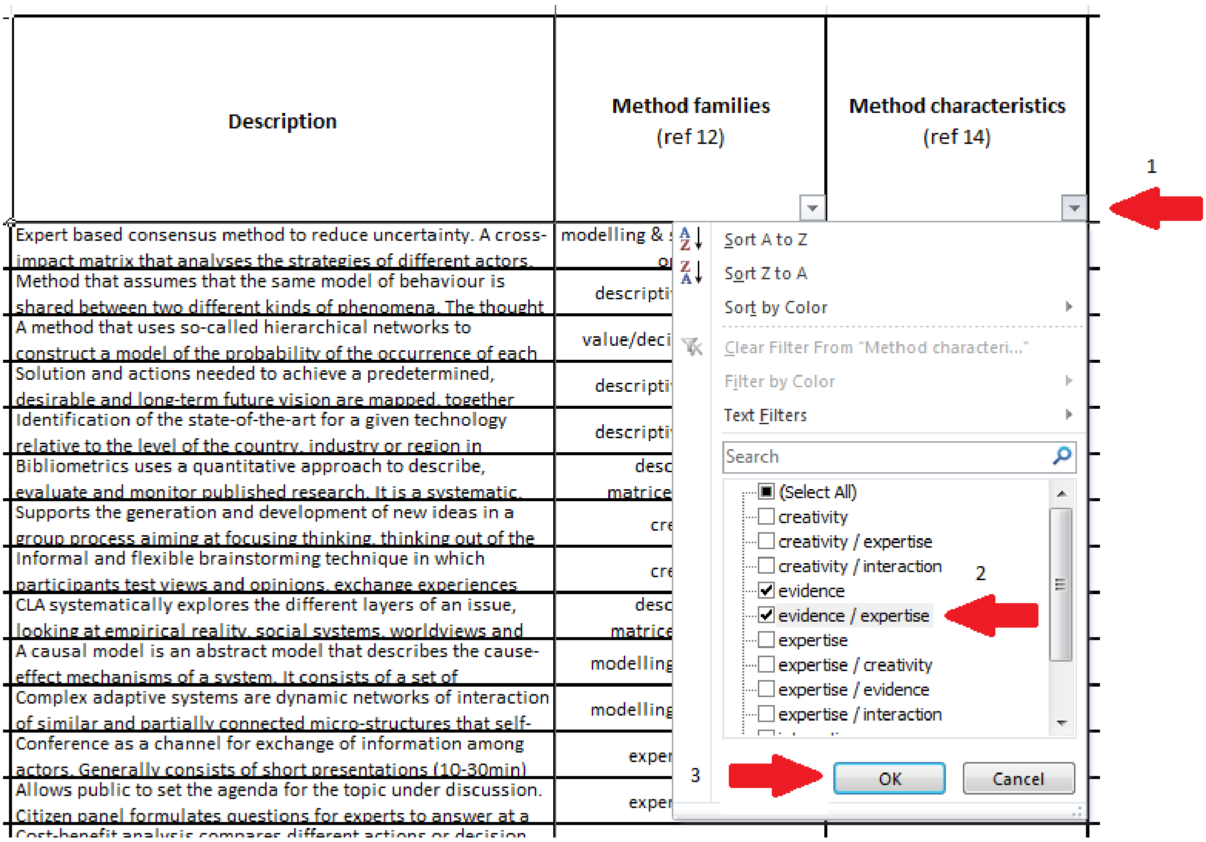

Figure 7. How to use the Excel-tool. 1) Click the arrow to open the filter options. 2) Select which characteristics should be included (tick box) or excluded (blank box). 3) Click OK to filter methods based on selected characteristics. It is possible to set multiple filters simultaneously. To remove filters, open filter options and choose "select all".

Do not forget to select “blank” as a filter option to include methods that do not fit one specific input. It is possible to filter different characteristics simultaneously, although filtering on too many characteristics might be imprudent, as this will restrict the selectable methods and result in tunnel vision.

Be aware that the Excel-tool does not list all available foresight methods, nor does it claim to be correct on all fronts. Most methods employed in foresight studies are highly flexible. Therefore, the assigned characteristics and descriptions are not set in stone, but can change depending on the study circumstances. The methods shown by the Excel-tool are suggestions only. In the end, it is up to the project team, in consultation with the client and/or stakeholders, to select which methods to use.

The information in the table relies mainly on the work of a number of authors, of which the references are stated below the Excel-tool. Furthermore, the "additional reading" column contains references to guides or other recommended papers. Any remaining empty fields were filled through comparison between methods and the author’s own insights. The categories "Method useful in uncertain environment", "Method useful in complex environment", "Objective families" and "Recommended time horizon" are mainly based on the author’s personal judgement, taking into account acquired knowledge of, but limited experience with, foresight methods and studies.

9.3. Building a method framework

There are many ways to combine selected methods into a framework. In a framework, one or more methods are used as input for other methods, resulting in the desired outputs. Some frameworks have more than one input-output layer. The goal of the framework is to interconnect methods and interconnect different types of knowledge to gain an interdisciplinary foresight study design[72]. Below are some examples of foresight study frameworks, starting with several frameworks from past RIVM foresight studies and finishing with an elaborate study design from literature.

Example framework: Dutch drinking water supply 2015-2040 (2014[54] and 2015[55] studies combined, see figure 8)

The following framework combines quantitative, evidence-based methods, with qualitative interactive methods from two successive foresight studies to think about potential drinking water supply developments and provide policy recommendations for making the Dutch drinking water supply more future-proof.

<u>Objectives:</u>

Study 1

- Determine future demand for drinking water in the Netherlands
- Determine need and possibilities for optimisation of drinking water supply

Study 2

- Determine is the Netherlands has sufficient drinking water capacity in 2040
- Suggest solutions for potential insufficient capacity

<u>Outputs:</u>

- Report

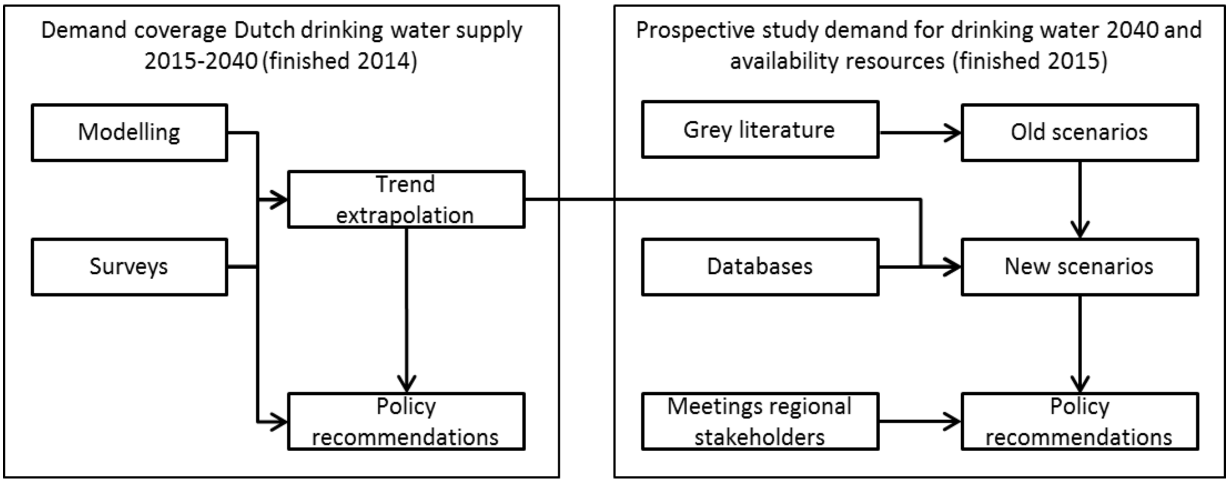

Figure 8. Framework for Dutch drinking water supply 2015-2040 combining two foresight studies. Left study: 1) Modelling of current and future drinking water supply. 2) Use model and drink water company surveys to extrapolate future trends. 3) Form policy recommendations using the demand forecast and available capacity. Right study: 1) Use literature to orientate on Dutch province policy regarding drinking water extraction. 2) Use old scenarios, updated by new information from databases, and extrapolated trends from study 1 to form min, trend, and max scenarios. 3) Make policy recommendations based on scenarios and meetings with regional stakeholders.

Example framework: The development of 3D printing – guiding visions towards a desirable future (see figure 9)

The following framework combines desk research with bilateral experts, developer and user interviews to extract barriers, drivers and visions related to 3D printing for consumers, healthcare, food and industry.

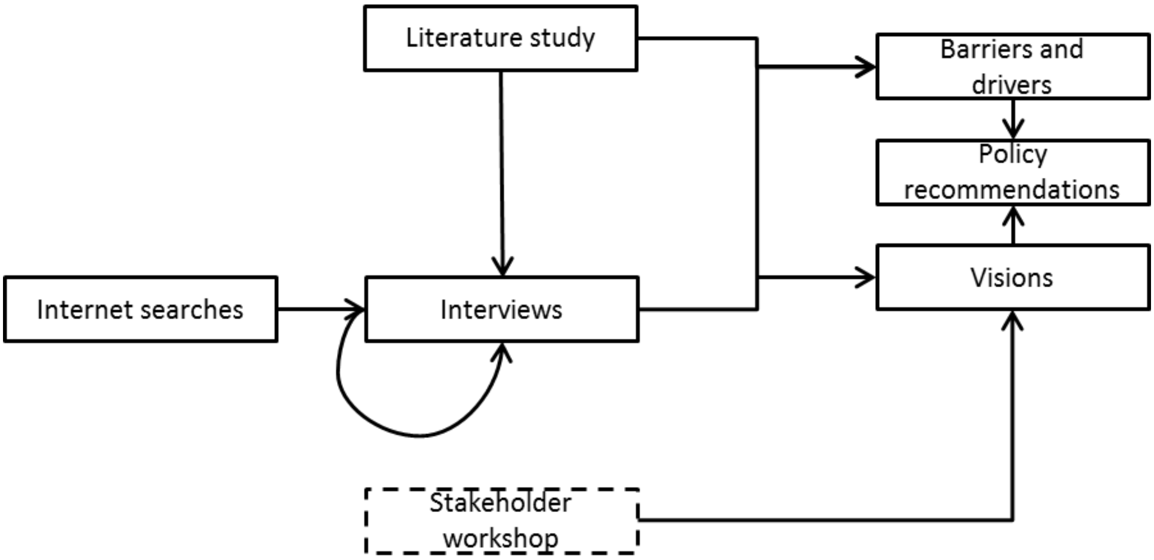

Figure 9. The development of 3D printing – guiding visions towards a desirable future. 1) Literature study to orientate on current developments, barriers and drivers, and to select interviewees, supplemented by internet searches. 2) Interviews to identify barriers, drivers, and visions, and to find more interviewees. 3) Form policy recommendations based on barriers, drivers and visions. 4) Stakeholder workshop to identify visions on printing in healthcare (organised after report was finished, additional method)

Objectives:

- Overview of current knowledge on developments and applications
- Identify developers and users of 3D printing
- Identification of conditions required for application development
- Map normative principles and visions of developers and users

Outputs:

- **Report**
- **Stakeholder workshop** (organised after the report to gain more insight in vision on 3D printing in healthcare)

Example framework: National research infrastructure roadmap[2] (see figure 10)

The following framework serves as an example of a large, multi-layered, national foresight study. Most likely, the RIVM would not perform such a study, but it gives an idea of how an elaborate framework can be build.

Goal:

- Identify research infrastructure requirements that will meet the countries' research needs over the coming two decades.

Objectives:

- Determine current and planned research infrastructure over a 20-year time horizon taking into account future opportunities and threats;
- Consider long-term sustainability of current research infrastructure
- Produce a detailed roadmap covering all main scientific disciplines with targets, milestones and recommendations
- Ensure commitment, engagement and participation of national stakeholders.

Outputs:

- National strategic roadmap
- Audit data on current infrastructure
- International benchmark results

Formulating a RI roadmap
Stage 1: (deskwork) audit and review (using a pre-defined set of indicators) of existing and planned RI in the country, and trend extrapolation and international benchmarking studies.
Stage 2: (deskwork) scenario writing with a view to setting out alternative futures.
Stage 3: expert panels generating a SWOT analysis and brainstorming ideas for future RI management and investments, followed by consultation workshops to gather views and validate findings of panels.
Stage 4: Experts formulating visions of RIs, and using these visions in a preliminary roadmapping exercise.
Stage 5: workshops to finalise & validate a national strategic roadmap for RIs.

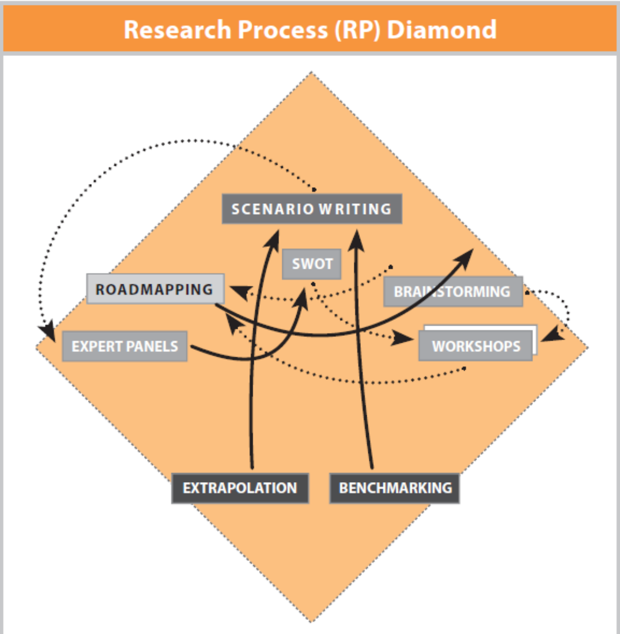

Figure 10. Framework for national research infrastructure roadmap represented in Foresight Diamond. (figure from [2])

10. Take-home messages for designing foresight studies

The design of a foresight study is characterised by three interconnected phases, which are the feasibility assessment, project scoping, and method selection. These phases are performed simultaneously and iteratively, together with the client and/or key stakeholders. Answers from the questions in the feasibility phase affect project scoping and method selection, just as scoping decisions on objectives and time horizon affect the answers to questions during feasibility assessment. Figure 11 gives a summary of the three phases.

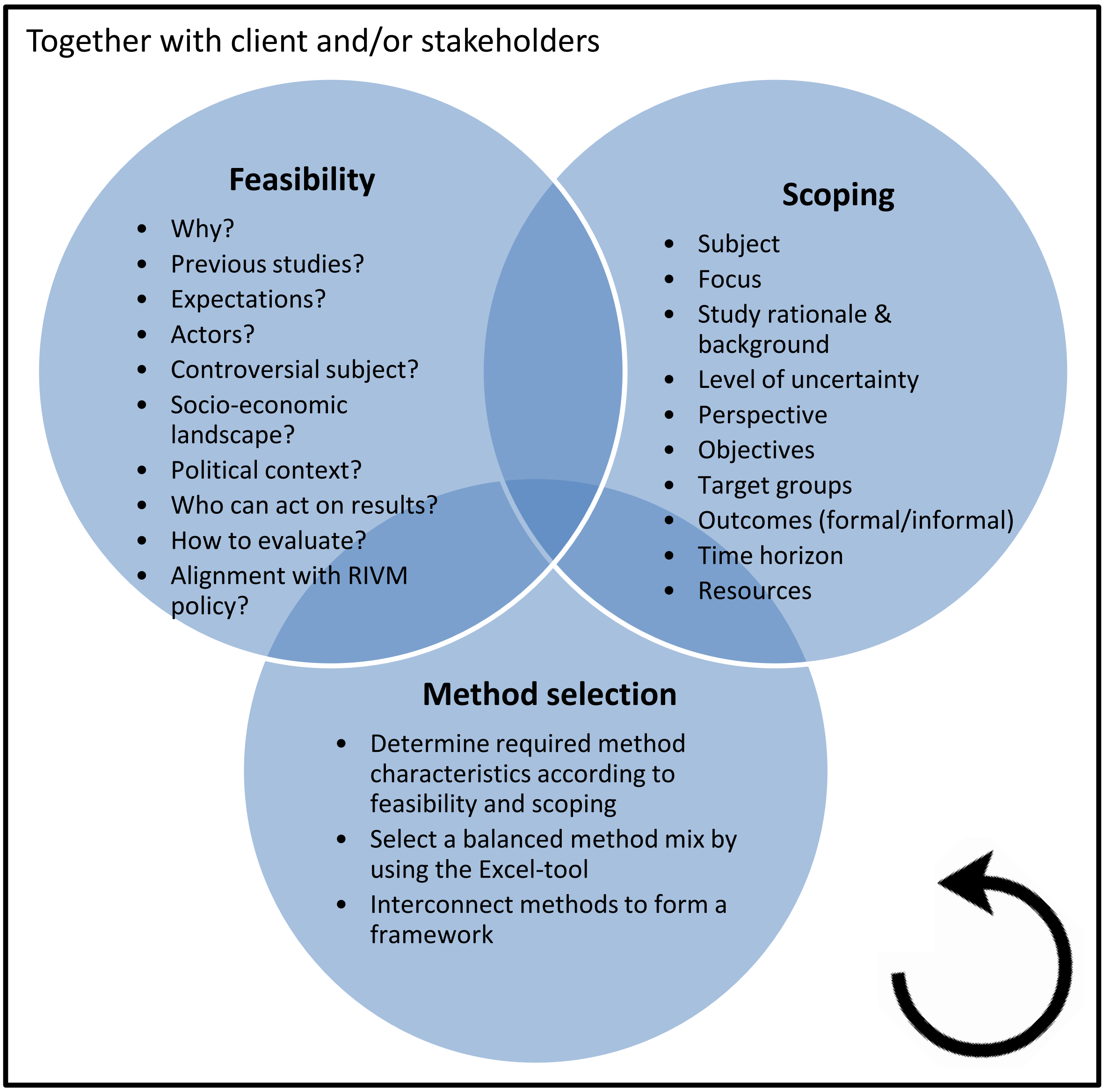

Figure 11. The three overlapping phases of foresight study design. Feasibility assessment, project scoping and method selection are performed simultaneously and iteratively, together with the client and/or key stakeholders. Making decisions in one phase will affect decisions in the others phases.

There are several take-home messages for designing a foresight study:

- Collaborate with the client and when necessary key stakeholders to design a foresight study that attempts to fit everyone's needs and wishes.

- Designing a foresight study is an iterative process that requires multiple rounds of open communication between the different parties.

- Choose a well-balanced mix of methods.

- Avoid the pitfall of technological determinism[41]. Technology is eventually used by society and therefore societal and normative aspects can play a large role in the future of technological innovations.

- The Excel-tool offers suggestions for methods to use. Due to the complexity and variation of foresight studies and the versatility of many methods you should feel free to deviate from the Excel-tool according to your own insights.

- Foresight studies are not the exclusive terrain of foresight experts[41]. Foresight practitioners from all skill levels are encouraged to conduct foresight studies, as practise is the best way to learn about foresight

Part 3 – Designing a foresight study on nanomedical devices

As nanomedical devices are a rapidly developing field with potentially a high future impact on the healthcare system the checklist document and method selection tool from Part 2 are used to design a foresight study for the RIVM.

11. An introduction to nanotechnology and nanomedical devices

11.1. Life at the nanoscale

Nanotechnology is the result of a convergence of many scientific fields, most prominently physics, biology, chemistry, electronics and engineering[73]. Nanotechnology is the deliberate design, characterisation, production and application of structures, devices and systems by controlling shape and size at the nanometre scale (1-1000 nm)[12]. A nanomaterial is a material with at least one external dimensions within the nanoscale[74], resulting in size-dependent properties that differ from individual atoms, molecules, and bulk matter[75].

Most definitions add that a material or structure should have at least one spatial dimension between 1 to a 100 nm to be considered a nanomaterial. However, this upper limit is established by consensus and according to the European Union's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) there is no scientific evidence to justify such a specific upper limit. Nanosized materials or structures above this range can still be considered nanotechnology when they exhibit unique properties, when compared to their micro- and macroscale counterparts. Furthermore, structures larger than 100 nm purposefully build from nanosized building blocks should still be considered nanotechnology[76]. Up to now, it has been difficult to design one definition that encompasses all types of nanotechnology and nanomaterials.

To provide some reference on size, 1 nm is one-millionth of a millimetre and comparable in size to molecules, like glucose (see figure 12). As materials become smaller, their total surface area relative to their size increases exponentially[77]. When materials become small enough different physical laws start to govern their behaviour than compared to bulk materials. Quantum effects, electrostatic interactions and van der Waals forces start to dominate and forces such as gravity become obsolete[78]. As a result, nanoscale materials and structures exhibit unique chemical, thermodynamic, electrical, mechanical, optical or biological properties when compared to their macroscale counterparts[79]. The presence of these unique properties as an effect of small size defines a nanomaterial.

In addition to size, the shape, or nanostructure, of the nanomaterial also influence its properties[78]. For example, graphene, buckminsterfullerene and carbon nanotubes are all composed of carbon atoms arranged in hexagonal structures (combined with pentagonal structures in case of the buckminsterfullerene). However, graphene is a flat 2D sheet; buckminsterfullerenes are spherical

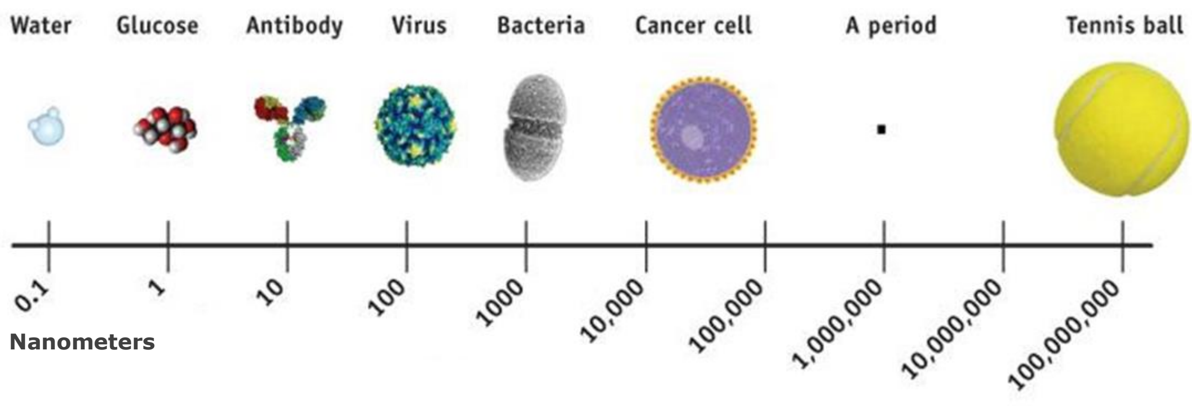

Figure 12. Scale depicting the relative size of nano-, micro- and macroscopic objects. (Adapted from the National Cancer Institute, http://nano.cancer.gov/learn/understanding/)

in shape, resembling a soccer ball; and carbon nanotubes are hollow tubes. Because of their different shapes, they have remarkably different properties even though all three have been made of the same atomic building blocks. Graphene has strong conductive properties[80]. Carbon nanotubes have excellent mechanical properties such as high elastic modulus and tensile strength[81], and can act as either conductors or semiconductors[82]. Buckminsterfullerenes are very stable and able to withstand high temperatures and pressures. Figure 13 shows a number of nanostructures. Nanoparticles are particles of any shape (e.g. shell, sphere, and prism) with all three spatial dimensions within the 1-100 nm range and defined physical boundaries. Nanotubes, rods, wires and fibres have two dimensions in the nanoscale range, while thin film, layers and coatings have only one dimension within 1-100 nm [82]. In addition to distinct nanomaterials, macroscale materials can also have a nanostructured surface topography made of nanometre structures.

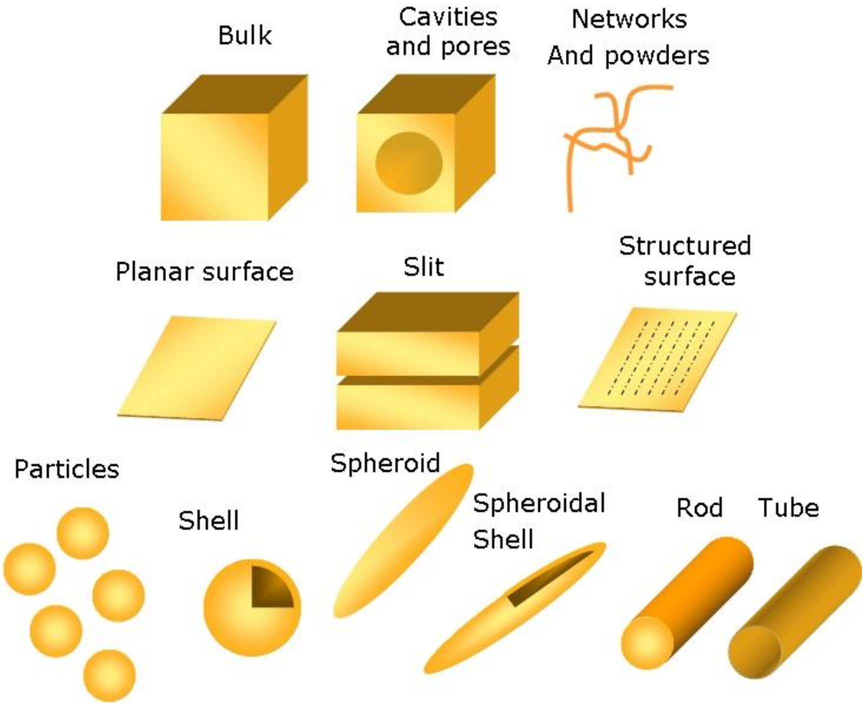

Figure 13. Different nanostructures encountered in nanotechnology (Figure from the Opensource Handbook of Nanoscience and Nanotechnology, https://en.wikibooks.org/wiki/Nanotechnology)

Nanomaterials can be either naturally occurring (e.g. proteins, viruses) or intentionally engineered and produced by a fabrication process. Natural nanomaterials are not considered nanotechnology, as they are not deliberately designed and produced by “controlling size and shape at the nanometer scale”. Most engineered nanomaterials are made either via a bottom-up approach where individual atom are combined to form a nanomaterial or via a top-down approach that reduces macroscopic materials to nanosized particles[83]. Examples of nanomaterials are nanocrystalline materials that consist of numerous nanosized crystalline domains; nanocomposite materials that contain two or more phase-separated components with nanosized dimensions; and hybrid nanomaterials made of organic and inorganic components interconnected at a molecular level[82]. Engineered nanomaterials are made from different materials and for a wide range of functions. Table 5 shows a nanomaterial classification used in the European Commission Compendium for Educators[82]. This classification sometimes results in the same kind of materials (e.g. nanocomposites) being described in separate groups (composites and nanocoatings made from nanocomposites).

Table 5. Different classes of engineered nanomaterials

Class	**Examples**
Biomimetic nanomaterials	Liposomes, micells
Carbon-based materials	Carbon nanotubes, graphene, fullerenes
Ceramic nanomaterials	Zeolites, aerogels
Composites	Inorganic nanocomposites, polymer nanocomposites
Nanocoatings	Superhydrophilic or hydrophobic coatings, responsive coatings
Nanostructured metals and alloys	Metal nanoparticles, nanocrystalline metals, ferrofluids, shape-memory alloys
Polymers	Conductive polymers, block copolymers, polymeric nanofibres
Self-assembled nanomaterials	Self-assembled monolayers, dendrimers, DNA nanostructures, liquid crystals
Semiconductors	Quantum dots, semiconducting metal oxides, photonic crystals

11.2. Nanomedicine: nanotechnology in healthcare

Nowadays nanotechnology and nanomaterials are found in a wide range of products. The European Union has named nanotechnology a ‘key enabling technology’ that drives technological innovation across multiple industries, such as in electronics, cosmetics, textiles and medicine[84-85]. The use of nanotechnology with the purpose of diagnosing, treating, monitoring or preventing disease is referred to as ‘nanomedicine’. This can be interpreted as the application of nanotechnology in healthcare[13]. Innovative applications of nanotechnology are increasingly used in the medical world and are expected to have a major impact on future healthcare through personalised medicine, miniaturisation induced cost reductions and the development of point-of-care applications, which allow fast near-patient diagnosis[86]. In addition, expectations are that nanomedicine will provide novel therapies for several major diseases, such as cancer, diabetes, neurodegenerative disorders and inflammatory diseases.

The field of nanomedicine consists of medicinal products and medical devices. Nanomedicinal products are substances containing nanotechnology used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis. These are often active pharmaceutical formulations with specific features designed at the nanometre scale[13, 52, 87]. These may be nanoparticle forms of the active pharmaceutical compound, nanoporous materials for controlled drug release, or nanoparticles acting as drug carriers either having the drug attached to their surface or encapsulated inside[52]. Examples of nanomedicinal products are iron nanoparticle contrast agents, quantum dot imaging agents, and drug-containing liposomes, micelles or dendrimers[52]. Nanotechnology allows for the fine-tuning of *in vivo* drug behaviour, leading to an optimal pharmaceutical effect[88]. For example encapsulating anti-cancer drugs in a tumour targeting liposome can increase treatment efficacy and reduce drug toxicity[89]. Naturally occurring nanosized macromolecules such as proteins and antibodies are not nanomedicinal products, as they are not purposefully designed according to the definition of nanotechnology. However, the engineered combination of an antibody with a drug or radioisotope is considered a nanomedicinal product[87].

Nanotechnology is also used in medical devices. A 'medical device' is defined as follows[90]:

> *Any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:*
>
> - *diagnosis, prevention, monitoring, treatment or alleviation of disease,*
> - *diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,*
> - *investigation, replacement or modification of the anatomy or of a physiological process,*
> - *control of conception,*
>
> *and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.*

Nanomedical devices span a wide range of products, including general medical equipment, in vitro diagnostics, and devices used by a wide variety of medical disciplines[13]. Table 6 shows several examples of existing nanomedical devices classified according to the categorisation employed by the RIVM[H]. Nanotechnology is used by incorporating nanomaterials as separate particles or scaffolds, by

[H] This categorisation was made during a RIVM project aimed at gaining an overview of nanomedical devices currently on the market. Due to the diversity of medical devices it is difficult to make a categorisation. Devices are used for treatment, diagnosis or both. Some are related to one disease or injury, while others are used in many. In this categorisation medical specialties were chosen as primary categories, with additional groups for nanomedical devices that do not fit one specific medical specialty. This categorisation might change or expand in the future due to the introduction of new nanomedical devices.

embedding nanoparticles in a bulk material, by creating a nanostructured surface, by adding a nanomaterial surface coating, by using nanosized electronic circuits and by employing nanofluidics. Nanotechnology and nanomaterials are used to improve the characteristics of existing medical devices or create entirely new ones.

Table 6. Nanomedical device categorisation and product examples

Nanomedical device category	Nanomedical device	Benefit of nanotechnology
Cardiology	Cobra PzF (nanocoated stent)[91]	Reduced thrombosis via promoted albumin binding
Dentistry	Filtek Supreme XT (nanocomposite restorative material)[92]	Improved wear resistance and aesthetics
Neurology	Artificial retina (in development)[93]	Miniaturisation
Oncology	NanoTherm™ (iron oxide magnetic nanoparticles)[94]	Magnetic field induced heat generation to kill tumour cells
Orthopaedics	NanoBone® (nanocrystalline hydroxylapatite bone substitute material)[95]	Promotes bone formation
Radiology	Carbon nanotube X-ray stationary digital breast tomosynthesis (in development)[96-97]	Carbon nanotubes as x-ray source
Diagnostic and continuous monitoring devices	Nanōmix system (carbon nanostructure biosensor for point of care testing)[98]	Miniaturisation
Surface modifications and coatings	HANANO™ (nanocrystalline hydroxyapatite implant coating)[99]	Improved anchoring strength and bone integration
Surgical instruments	ENSEAL® G2 Tissue Sealers (conductive nanoparticles)[100-101]	Thermostatic switch to regulate heat transfer
Textiles and wound care products	Nanogen Aktiv (nanofiber cellulose wound membrane)[102]	Biomimetic scaffold

11.3. Medical device regulation in Europe and borderline products

The European regulatory framework for medical devices (including medical devices containing nanotechnology) consists of three European Commission directives: 90/385/EEC on active implantable medical devices[103]; 93/42/EEC on medical devices[90]; and 98/79/EC on *in vitro* diagnostic medical devices[104]. Several implant scandals fuelled the debate for a revision of the European regulatory framework. In 2012, the European Commission published a proposal for a new medical device regulation and a new *in vitro* diagnostic medical device regulation. Final versions are not expected in the near future[105].

As described in 12.2, medical devices are a diverse group of products ranging from plasters and hospital beds to complex devices such as deep-brain stimulators and MRI scanners. The European regulatory framework is based on the categorisation of medical devices in separate risk classes according to legally defined rules. Medical devices in higher risk classes face more strict assessment procedures to obtain market entry. In Europe, Notified Bodies (NBs) perform these market entry procedures. NBs are companies, specifically designated for this task and supervised by the government[105].

The classification system distinguishes low, medium, and high-risk medical devices. The assigned risk classification determines which approval procedure has to be followed to gain market entry. The European system has four risk classes: I, IIa, IIb and III. A medical device is classified in one of these groups according to criteria such as the duration of use, invasiveness, place of contact, biological effect, and energy supply[105]. Figure 14 shows some examples of medical devices per class. All medical devices incorporating or consisting of nanomaterial deliberately intended to be released into the human body are considered a class III device[106]. Only class IIa/b and class III devices require a conformity assessment procedure by a NB. Most class I medical devices are assessed by the manufacturer itself. After conformity has been established the NB issues a CE certificate. Registration of the device with a Competent Authority is necessary before placing the device on the market[105].

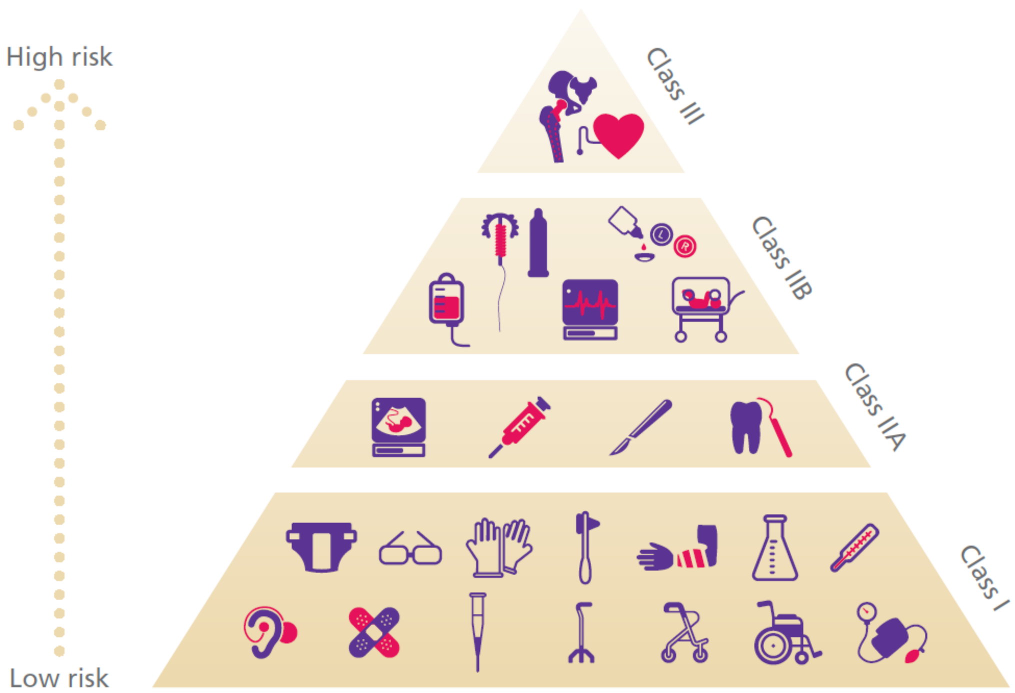

Figure 14. Examples of medical devices per risk class. (figure from [1])

Regulatory difficulties can arise when a product meets both the definition of medicinal product and medical device, for example in drug/device combinations. However, a product cannot fall under both medical device regulation and medicinal product regulation. Therefore, when the product in question falls within the definition of both, the product is classed as a medicinal product[107]. European regulation defines a 'medicinal product' as follows[108]:

(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or

(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis

A product constitutes a medicinal product if either regulation a), b) or both apply to it[107].

An example of regulatory ambiguity is the difference in regulation between injectable iron oxide nanoparticles used for heat therapy in cancer treatment and ultra-small superparamagnetic iron oxide nanoparticles (USPIONs) injected as a MRI contrast agent in diagnostic imaging. The iron oxide nanoparticles for heat therapy are registered in Europe as a medical device[94], while USPIONs used in imaging are registered as medicinal products[109]. Both types of iron nanoparticles do not perform their primary mode of action through pharmaceutical, immunological or metabolic means but via a physical action, be it either heat or optical contrast. However, as USPION contrast agents are administered to human beings to make a medical diagnosis, they are registered as medicinal products.

For drug/device combinational products one takes into account the principal mode of action to determine if the product should be classed as a medical device or medicinal product[107]. Deciding what the primary mode of action is can sometimes by difficult, creating problems for classifying a product as either a nanomedicinal product or medical device. A drug/device combination is considered a medical device if the accompanying drug only has an ancillary action, but is not responsible for the primary purpose of the combinational product. An example is a wound dressing containing silver nanoparticles. The principal intended action of the wound dressing is covering the wound and providing a barrier to bacteria. The silver nanoparticles, a medicinal product, provide auxiliary support by further reducing the possibility of infection. If the principal intended action was to get the silver nanoparticles to the wound, and the dressing would just serve as a drug carrier, the product would be regulated as a medicinal product[107].

11.4. Toxicity and risk assessment of nanomaterials

As mentioned previously, nanomaterials have specific characteristics that are different from bulk substances of the same chemical composition. However, as nanomaterials are of the same size as the building blocks of biological systems (e.g. proteins, DNA) these new characteristics might lead to unexpected interactions with biomolecules, cells, organs and organisms[13]. As a result, exposure of humans and the environment to nanomaterials might cause unforeseen adverse effects. Nanomaterials are not by definition toxic, but can have unknown adverse properties because of their chemical composition, size, and shape[13]. Scientific research on new nanomaterials and nanotechnologies, and the use of these in commercial products outweighs the current knowledge on safety and potential toxicological effects of nanomaterials in humans[l].

Potential toxicological effects of nanomaterials depend on their absorption, distribution, metabolism and excretion pattern. The tissue-specific distribution, accumulation and elimination of nanomaterials is considered more relevant than total blood plasma levels, as free nanomaterials are

[l] A quick keyword/title/abstract search in Scopus for articles or reviews on 17-6-2015 resulted in 849,580 documents for nano* and 28,206 documents for nano* and *toxicity. (Pubmed: 32,824 nano* vs 2008 nano* AND (toxicity OR cytotoxicity) (title/abstract, article or review)).

often quickly cleared from the blood[110]. The spleen and liver are likely the main responsible organs for clearing nanomaterials from the blood, resulting in organ accumulation[111-113]. Inhaled nanomaterials mostly end up in the lung[114]. In addition, they may partly end up in the gastrointestinal tract or may migrate to the brain via the olfactory nerve[115-116]. Nanomaterial absorption following dermal exposure is generally considered low or absent, but increases when the skin is damaged[117]. Implanted medical devices most likely generate minor quantities of free nanomaterials, with the exception of the wear-and-tear seen in hip prosthesis[110]. After subcutaneous injection of nanomaterials in mice, a model for implant-released nanomaterial distribution, most particles were found in draining lymph nodes, and to a lesser extent in the lung, liver and spleen[118].

The potential toxic effects of nanomaterials depend on their concentration, chemical composition, size, surface area, electrical charge and structure, among others[119]. Due to their high surface-to-volume ratio, nanomaterials have a very reactive surface. When introduced to the body, proteins and biomolecules form a corona around the nanomaterial's surface. This corona determines part of the interaction between the nanomaterial and the biological system on a cellular and molecular level[120]. Nanoparticles are able to interact with the cell membrane, resulting in for example endocytosis or cell membrane penetration. Cell membrane penetration creates membrane pores, potentially causing cytotoxicity via imbalances in ion, protein or macromolecular concentrations[121] or by damage to mitochondria[119]. Nanomaterials can also induce the generation of reactive oxygen species, resulting in DNA damage, cytotoxicity, apoptosis, and cancer initiation[122-123]. Furthermore, nanomaterials can induce inflammation, for example when nanoparticles accumulate in the lung[110].

Nanomedical devices can also expose patients to nanomaterials in one form or the other. This can be as free nanoparticles administered directly to the patient (e.g. iron oxide nanoparticles for tumour hyperthermia), nanomaterials in paste-like formulation (e.g. dental filling nanocomposites), free nanoparticles added to a medical device (e.g. silver nanoparticles in wound dressings), implant nanocoatings, nanomaterials that are degraded over time, or nanomaterials embedded within a bulk material. In addition, some medical devices that by themselves do not contain nanomaterials can create them during use (e.g. nanoparticles from wear-and-tear of hip prostheses)[110]. Depending on the use of the nanomedical device, the patient can be exposed to nanomaterials in several ways, such as by skin or mucosal contact, inhalation, oral ingestion, direct implantation, or injection.

The SCENIHR recommends estimating the external and internal exposure potential according to the type of device (surface, inserted, or implanted), the type of application of the nanomaterial (free, fixed, or embedded), the type of contact (intact skin/mucosal, breached surface, tissue/bone/dentin, direct/indirect blood contact) and the duration of contact (≤24h, >24h-30d, >30d)[110]. As examples, a surface device having fixed/embedded nanomaterials in contact with intact skin for shorter then ≤24h is marked as having negligible internal exposure potential. However, an implanted device containing free nanomaterials in contact with the blood for >30d is seen as having high potential internal exposure. Eventual risk evaluation should be done on a case-by-case basis according to a four-phased approach taking into account the nanomaterials characteristics and potential for nanomaterial release and exposure. The four phases are 1) Particle release, 2) Particle distribution and persistence, 3) Toxicological evaluations, 4) Risk assessment.

11.5. Necessity to anticipate future developments in nanomedical devices

As discussed above, it appears that developments in nanotechnology are outrunning both policy regulations and knowledge on safety issues. The same is the case for nanomedical devices. As nanomedical devices are rapidly developing and potentially have a high impact on healthcare and society it is important to anticipate potential future developments within this field. Therefore, it is important for the RIVM's role as government advisor to gain insight in the short and mid-term developments of nanomedical devices and their potential opportunities, risks, and impacts on healthcare and policy. This importance is illustrated by recent questions from the Dutch Ministry of Health, Welfare and Sport (VWS) and the Dutch Healthcare Inspectorate (IGZ) on current and future developments within the field of nanomedical devices. To address these questions the following chapter designs a foresight study according to the developed checklist document and Excel-tool.

12. Designing a foresight study for nanomedical devices

12.1. RIVM project on nanomedical devices provides boundary conditions

The foresight study for nanomedical devices will be designed according to the checklist document and Excel-tool from Part 2 of this report, resulting in a method framework. A current RIVM project on nanomedical devices provides the boundary conditions for designing the study. The VWS and IGZ are the project's sponsors. The project tender[J] provides financial resources to a maximum of €75.000 and a timeframe of one year. The tender states the following objectives and outputs:

- Provide an overview of nanomedical devices currently on the market or expected within 5 years;
- Determine if trends exist for specific categories of nanomedical devices;
- Identify nano-related opportunities and risks of the different categories of nanomedical devices;
- Identify the most important gaps in scientific knowledge to make a good benefit-risk assessments;
- Actively communicate relevant findings to the appropriate target groups;
- The results will be presented in a report or policy-relevant publication for both project sponsors.

12.2. Feasibility assessment

This section answers the questions stated in Chapter 7 to assess the feasibility of the intended foresight study and gain more insight into its context.

Why are we conducting a foresight study?

Innovative medical applications containing nanotechnology will likely have a major impact on healthcare in the future. These applications will lead to new possibilities for diagnosis, treatment, monitoring and prevention of diseases, disorders, and disabilities. In addition to the field of nanomedicinal products, it is expected that the field of nanomedical devices has progressed rapidly after the last RIVM foresight report on this subject was published in 2005[124]. For the Dutch government it is strategically important to gain insight in the opportunities and risks connected to new nanomedical devices, as these could warrant changes in policy or regulation, changes in healthcare inspection, and have an impact on the current healthcare system.

What is the added value of the foresight study?

Nanotechnology is a hot topic, but foresight studies specifically on nanomedical devices are very scarce (see below). The current foresight study would therefore offer value as one of the few foresight studies directed specifically at nanomedical devices. It can provide a broad overview of nanomedical devices on the market, something that is currently missing in literature. Furthermore, projecting on expected short-term developments can assist policymakers, healthcare inspectors, healthcare workers and patients in preparing for potential future developments and their associated

[J] Due to confidentiality issues, it is not possible to present the complete tender as an appendix.

impact on the healthcare system and society. Additionally, this foresight project provides the opportunity to connect the different stakeholders on nanomedical devices to identify and communicate opportunities and risks of the different nanomedical device categories.

The foresight study might not add value to the identification of the most important gaps in scientific knowledge to make a good benefit-risk assessment, as the recent SCENIHR opinion adequately addresses the risk assessment of nanomedical devices[110].

What activities or studies on the same subject are already done or on-going?

Scientific reviews describing current developments in nanomedical devices and providing future projections are available for some of the nanomedical device categories and product groups (e.g. dentistry[125], implants[126]). A non-exhaustive Google and Bing internet search resulted in three foresight studies and several market reports published since 2010 (keywords foresight OR future, study, nanotechnology AND medical device OR nanomedical device). These studies are usually a mixture of medicinal products and medical devices:

- *Economic Foresight study on R&D for the European Industry - Economic foresight study on industrial trends and the research needed to support the competitiveness of European industry around 2025*, European Commission and Fraunhofer Society, 2012[127]

  Foresight study on nanosciences, nanotechnologies, materials and new production technologies (NMP) with an economic focus. The study identifies past trends, and current and prospective drivers for the economic development of NMP, including nanomedical devices. The study uses a quantitative model, supplemented with qualitative key factors to create different future scenarios of NMP's effect on the European industry around 2025.

- *Nanotechnology Research Directions for Societal Needs in 2020 - Retrospective and Outlook*, WTEC Panel Report, 2010

  The report describes the expected targets for nanotechnology R&D in the next decade, and how to achieve them in the context of societal needs and other emerging technologies. The report incorporates views of experts from academia, industry, and government shared among representatives from 36 countries gathered via four multinational forum meetings. The report is aimed at stakeholders involved in planning R&D programmes on nanotechnology.

- *Nanomedical Device and Systems Design: Challenges, Possibilities, Visions,* Frank Boehm et al. book, 2013

  Book going into the challenges encountered in designing envisaged nanomedical devices of the future. The book contains several chapters on current developments written by experts in the field.

- Several market reports containing economic forecasts and description of products and companies. These reports almost always contain a mix of medicinal products and medical devices.

Can I make use of these studies?
The first two studies provide information on drivers of economic development and expert visions on R&D developments. Both of these are not objectives of the current foresight study, so they only function as useful background information. Furthermore, they do not specifically focus on nanomedical devices. The book and market reports can provide examples of current products and future developments, however both have to be bought, with the book costing €180,- and the market reports costing around € 5000,-. Experience with a recent market report on nanomedicine showed that most of the product information was out-dated.

How can I differentiate from these studies or add additional value?
The foresight study already differentiates itself from other studies by focusing solely on nanomedical devices. A comprehensive overview of current products on the market is missing in literature. Furthermore, the foresight study can differentiate itself by focusing on nanotechnology related opportunities and risks in all categories of medical devices. None of the abovementioned foresight studies communicates with citizens, patients, clinicians and/or other stakeholders, providing an opportunity for this foresight study to differentiate itself.

Who is the main client or sponsor of the foresight study?
This foresight study has two main clients. These are the Ministry of Health, Welfare and Sport, and the Dutch Health Care Inspectorate. Both clients have given the RIVM the same questions and objectives. However, the Ministry is more interested in opportunities related to nanotechnology in medical devices, while the Inspectorate is more interested in the associated risks.

What are the expectations of the client towards the foresight exercise?
Only the expectations explicitly stated in the tender are known. Further consultation will be necessary to determine other expectations.

How will the client use the results of the foresight study?
It is likely that the clients will use the results to prepare themselves for future eventualities within the field of nanomedical devices. Ideally, the results on opportunities, risks, and expected future products will help in formulating public policy to mitigate risks and prepare the healthcare system for new nanomedical devices. However, further consultation will be necessary to determine the clients' viewpoint on these matters. In addition, it will depend on the results of the foresight study.

Who are the main actors related to the subject of the foresight study?
The main actors in relation to this foresight study are:

- IGZ
- VWS, Directorate of Medicines and Medical Technology (GMT)
- RIVM, Department of Product Safety, Centre of Health Protection
- RIVM KIR-nano (Risks of Nanotechnology Knowledge and Information Centre)

- NanoNextNL (Dutch consortium of universities, companies, and medical centres on nanotechnology research)
- National Platform Nanomedicine (NPN, NPNDutch platform for people involved in nanomedicine)
- Notified bodies in Europe (European medical device registration class II and III)
- CIBG/Farmatec (Dutch medical device registration class I and *in vitro* diagnostics)
- Dutch and international universities and research institutes
- Patients
- Clinicians
- Health insurers
- Nanomedical device industry

Additional actors within the field of nanomedicine and nanomedical devices surrounding the current foresight study:

- European Commission / European Union (Legislative authority and controls EUDAMED, an incomplete and non-accessible database on medical devices in Europe)
- European Foundation for Clinical Nanomedicine (CLINAM, has an annual international congress on nanomedicine)
- European Technology Platform Nanomedicine (industry initiative to coordinate joint European research efforts on translation of nanomedicine from bench-to-bedside)
- ISO/TC194 Biological Evaluation of Medical Devices working committee
- ISO TC 229 Nanotechnology working committee
- EC New & Emerging Technology Working Group
- European Association of Notified bodies for Medical devices (Team-NB)
- European Medicine Agency ((nano)medicinal product regulation)
- College ter Beoordeling van Geneesmiddelen (Dutch regulative authority of (nano)medicinal products)
- Dutch and international universities and research institutes
- Confederation of Medical Devices Associations (EUCOMED)
- Alliance of European Medical Technology Industry Associations (MedTech Europe)
- European Diagnostic Manufacturers Association (EDMA)
- Diagnostica Associatie Nederland (DIAGNED)
- Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)

To identify additional actors a brainstorm session with the team and client could be organised. This list of actors and/or stakeholders is rather broad and it is not specified who the acting persons are.

What position does each actor take?

A number of Dutch actors has been categorised according to a power/interest matrix[128] (see figure 14). This matrix is about the power and interest of different actors regarding nanomedical devices. This is a concept version, but can provide some bearing on the importance of different actors. A more definitive version, with additional actors, should be made during a discussion session together with the client.

Actors in the lower left-hand corner are the least important stakeholders and should be informed of the results or process. Actors in the lower right-hand corner should be informed and involved in low risk areas. Actors in the top left-hand corner have high power, but low interest. Their interest should be increased by engaging and consulting them on their specific areas of interest. In the top right-hand corner are the key players. These should be directly involved in governance and decision making in the foresight study. To keep these actors in this corner they should be engaged and consulted regularly.

Are there key stakeholders that should be involved in the study?

There do not appear to be additional key stakeholders, apart from the current clients.

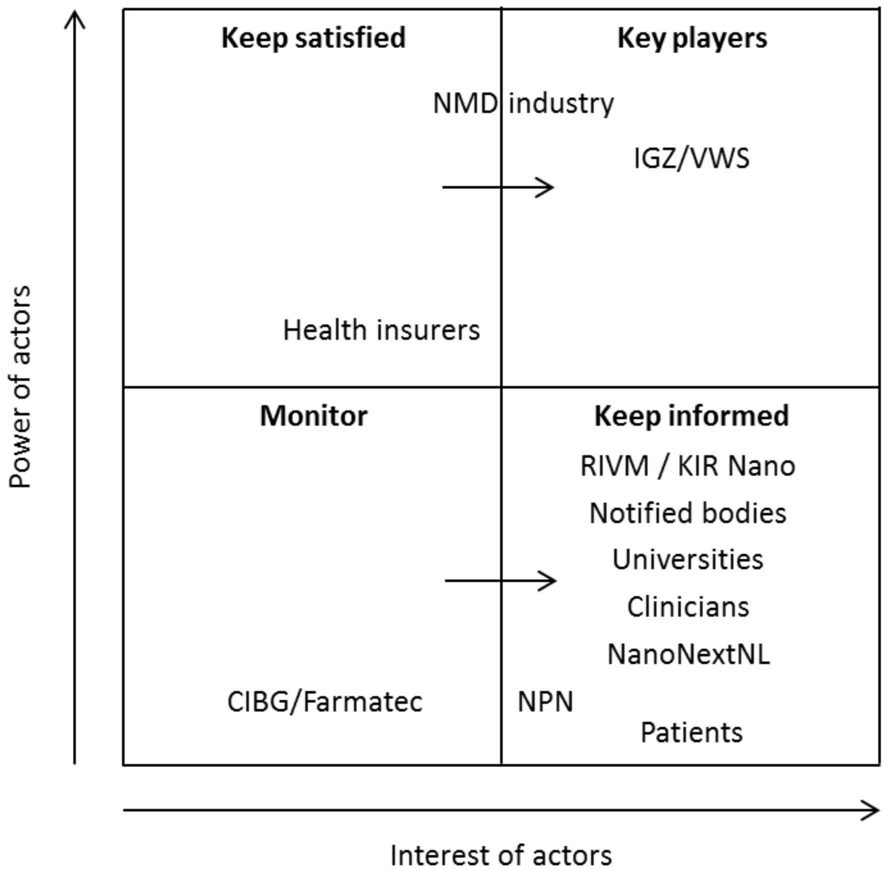

Figure 14. Power/interest matrix. The aim is to move parties from the left-hand side to the right-hand side by increasing their interest in the study.

Which actors are under your control or influence, and which are not?

KIR Nano is directly under the control of the RIVM. In addition, the RIVM can influence several actors, such as the Dutch Nationaal Platform Nanomedicine, the ISO working committees, Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), and the EC New & Emerging Technology Working Group. The other actors are more difficult to influence.

Which actors can help the foresight study? Which actors might oppose it?
Helping actors might be clinicians, and scientific and governmental organisations. There do not appear to be directly opposing actors, but it is possible that not all industry organisations and notified bodies are willing to help the study due to their own commercial interests.

Are there initiatives or agendas that could influence the foresight study, in scoping, need for timing or cooperation?
The European Commission is working on a new medical device regulation and *in vitro* diagnostic medical device regulation. A proposal was published in 2012, but the final version is still under negotiation[105]. Although the current foresight project is for the Dutch government, its findings could potentially influence the development of new regulation. For example when new nanomedical devices are expected to cause difficulties under the current regulation, the Dutch government can use this to try and influence the new European regulation.

Which of the actors is in a position to act on the result of the foresight study?
The VWS and IGZ can act on the results of the foresight study, as it concerns an internal report. However, the report might be transformed to a public RIVM report at a later stage. In this case, patients, clinicians, industry and other governmental or non-governmental organisations can use the results. VWS, IGZ and the European Commission can act on the results. In addition, clinicians can act on the results by becoming aware of specific nanomedical devices for use now or in the future.

Is there enough support for the foresight study?
There appears to be enough support for this foresight study among the relevant actors.

What kind of techno and socio-economic landscape surrounds the subject?
Nanomedicine is a field in rapid technological development. It is influenced by new discoveries in a number of scientific fields (biology, chemistry, engineering, physics, nanotechnology etc.). It is a high-tech manufacturing sector, in which the United States is the clear frontrunner in terms of scientific publications, followed by China, Germany, the United Kingdom, and India (Netherlands is in 15th place)[K]. National governments and the European Union sponsor a high number of research and product development programmes with large amounts of subsidies. Nanotechnology is expected to be one of the important drivers of the European economy[127].

As often seen in dynamic and innovative technological fields governmental regulations are lagging behind. There is still much uncertainty on safety aspects and potential long-term health and environmental impacts along the whole value chain and life cycle of nanomedical devices.

Nanomedicine is expected to revolutionise healthcare. Products are starting to enter the market, but for most device categories, it is still in an early growth phase. It is unclear how aware ordinary citizens are of nanotechnology and nanomedicine developments. There is currently no societal protest against nanomedicine, but a scandal with an early product can cause public opinion to turn for the worst, resulting in potential problems for all medical products incorporating nanotechnology.

[K] Scopus search on 18-6-2015 on nano* AND medicine in title/abstract/keywords from 1995 to 2015. Scopus allows for analysing the search results, based on country of publication.

Is the subject's landscape characterised by conflict or complacency?

The subject's landscape is characterised more by conflict than complacency, although it appears that all actors are on speaking terms. Governmental organisations are focussing on the unknown safety aspects of nanomedicines. The RIVM is promoting a safe-by-design concept in which safety becomes an important aspect during the design phase of nanotechnology containing products. On the other hand, the industry is already marketing products and has until now less regard for the safe design of their products than other parties. However, high risk medical devices (containing free nanomaterials) still have to go through stringent safety testing. The European legislative authority tries to balance safety against innovation and economic growth. However, recent scandals involving medical devices (e.g. breast implants, transvaginal meshes) have prompted them to break open the current regulatory system.

Is there a culture of collaboration?

There is a culture of collaboration surrounding nanotechnology as shown by the many consortia and platforms, such as NanoNextNL and the European Technology Platform Nanomedicine.

What is the general attitude of the landscape towards foresight studies?

The European Union regularly conducts foresight studies on a broad range of subjects. Furthermore, the Dutch authorities also have a history of conducting foresight studies. It is unknown how active other actors are in this regard.

Is the subject of the foresight study potentially controversial?

The subject is not necessarily controversial. However, recent regulatory scandals involving PIP breast implants and transvaginal meshes have gotten considerable media attention. As a result, safety regulations are likely going to be tighter in the new European medical device regulation. Considering the remaining unknowns about nanotoxicology and safety, this might become an important societal topic in the future.

What is the political context of the foresight study?

The European medical device regulation is currently under revision. The Dutch political position is that nanotechnology-related opportunities cannot be seized without controlling the risks. However, the European Union should formulate policy regarding the handling and judging of human and environmental risks. The Dutch government tries to influence European policy development[129]. There is no specific statement on nanomedicine or nanomedical devices.

Who are the main political actors with regards to the subject?

- The European Council, which is updating the medical device regulation, while balancing economic growth and innovation against safety.
- VWS is interested in the economic and healthcare benefits of nanomedical devices. VWS can try to influence decision-making at a European level.
- IGZ, which is more focused on the potential risks of nanomedical devices.
- The RIVM can attempt to influence the process via several European working groups.

What is the political culture surrounding the subject?
Nanotechnology is not a major political subject in the Netherlands.

What is the position of the foresight study in the policy cycle?
The foresight study might put nanomedicine on the policy agenda of VWS when it appears that potential future nanomedical devices can cause regulatory problems or heavily impact the healthcare system.

Is the political environment stable or instable?
The political environment surrounding the subject appears stable.

Can the study link up with already ongoing activities or agendas?
The study could link up with a current RIVM foresight study on nanomedicinal products by organising interactive methods together and sharing results and experiences. It is unclear if there are other national meetings, workshops, projects, or foresight studies ongoing on the subject of nanomedical devices. During the study, the project team should stay vigilant towards such events as they might provide an opportunity or threat.

Can policy-makers be directly involved in the design or execution of the foresight study?
Yes, it is necessary to involve VWS and IGZ policy-makers in both the design and execution of the foresight study as this will enable direct learning, communication and meeting of expectations.

Is the foresight study aiming for a certain policy implementation?
Not directly.

How will you generate policy support for the foresight study?
By actively involving the foresight study clients, VWS and IGZ.

What do you want to achieve with the foresight study?
The project team wants to achieve an overview of nanomedical devices currently on the market. This overview cannot be exhaustive, but should ideally include as many product groups as possible. Furthermore, they want to identify one or more trends in products that are likely to appear on the market within 5 years. The study should identify nano-specific risks and opportunities per category or product group of nanomedical devices. The project team wants to actively communicate relevant findings to appropriate target groups through an interactive gathering of relevant actors/stakeholders.

When are you and the client satisfied with the results?
The project team is satisfied with the results if the project stays within the budget and timeframe; can provide a comprehensive overview of nanomedical devices currently on the market; and have actively interacted with societal actors regarding future developments. It is unclear when the client will be satisfied with the results.

What are the measureable outcomes?

- 1 internal report for VWS and IGZ
- 1 gathering with relevant actors and/or stakeholders

How are you going to evaluate the foresight study?

The foresight study will be evaluated together with the clients on the following subjects: internal and external communication, study preparation (feasibility assessment, scoping, method framework), methods and their implementation, positive and negative experiences, outcomes (report content), time and money spent, and alignment with RIVM and client policy.

Are there enough resources to conduct the foresight study and gain valuable results?

Yes

Are the necessary capabilities available to conduct the foresight study?

Capabilities are available to conduct desk methods. Perhaps additional competences from outside of the project team have to be obtained to conduct interactive and creative methods. These competences will be sought within the RIVM to prevent the need of hiring external parties.

How do we align the study with RIVM policy?

This foresight study will be aligned to RIVM corporate policy by making contact with society through interactive methods with relevant target groups. Which target groups are relevant will be decided in consultation with the clients.

Are there additional RIVM policies or strategies influencing this foresight study?

The RIVM strategy on risks of nanomaterials 2013-2016[129] influences this foresight study. This document involves a communication strategy on the risks of nanotechnology. This communication strategy states that the RIVM should move from providing information (sending) to open dialogue (exchange). However, the RIVM should stay clear of persuading for a specific standpoint. The overall nanomaterials strategy states that more emphasis should be placed on the process, in addition to the content. In short the strategy states that the RIVM aims to integrate knowledge across existing boundaries; speed up the process of risk assessment; and participate in the whole nanotechnology innovation chain. The foresight study might assist in this last aim by connecting with a current RIVM project on safe-by-design and interact directly with innovative nanomedical device companies.

How do we connect to society with this foresight study?

This study can connect with society by interacting with companies, clinicians and/or translational researchers to determine the types of nanomedical devices that are likely to become available within the next 5 years. Furthermore, by directly involving the clients in this process potential regulatory difficulties can be discussed and active learning is promoted.

How do we capture and secure relations?

By actively using the existing RIVM network in nanomedicine the project team can strengthen and maintain these relations.

Are we going to collaborate with internal or external multidisciplinary parties?
Perhaps the project team can collaborate with the safe-by-design RIVM project on safety in nanotechnology innovation.

How are we going to be more proactive and show guts?
We will be more proactive by actively connecting relevant actors and stakeholders with policy-makers to engage in individual and organisational learning, and future thinking.

12.3. Scoping

This is a first blueprint of scoping, which should be further discussed with the client.

Project focus
The focus of this foresight project is on nanomedical devices and technological developments, risks and opportunities within this field. Economic potential or societal norms and values are not the focus of this study. In addition, regulatory or policy related matters are not the primary focus, but when specific products, technological developments, risks or opportunities might potentially affect regulation or policy this will be noted.

Organisational focus (e.g. method participants) will be on the Netherlands and possibly Europe, however when determining current and potential future nanomedical devices the focus shifts to worldwide. The reason for this is that nanomedical devices being developed or brought on the market in other countries (e.g. the United States) can relatively quickly also enter the European market. When the focus would only be on Europe, important nanomedical devices might be missed that can impact the Netherlands on the short-term.

The level of detail will be mostly on product groups (broad) and not specific products. However, specific products can be used as an illustrative example for the whole product group. Furthermore, when specific products appear to have a large future impact they might be specified upon.

Perspectives and types of uncertainties
The future of nanomedical devices is dynamic, unstable and unpredictable, as with most rapidly developing technological fields. New developments in related fields (e.g. nanoelectronics, nanomaterials) can relatively quickly spread across the field of nanomedical devices. The field of nanotechnology is too diverse and widespread to oversee. Furthermore, many devices are developed out of public view within companies, making it difficult to anticipate potential game changers. As a result quantitative methods are not useful and qualitative methods are more appropriate.

The foresight study has a technological perspective, while keeping in mind potential regulatory or healthcare related impacts.

Normative or societal uncertainty is not taken into account during this foresight study, as cognitive uncertainties are considered much larger, both on new nanomedical devices and on their potential opportunities and risks. Furthermore, all stakeholders support the same desirable future where nanomedical devices result in better and cheaper healthcare. This is a generalisation, as some actors might have additional motives (e.g. financial, public interest, risk minimalisation). A more specific foresight study might be conducted on the normative values concerning specific nanomedical devices or product types if there is reason to do so, but for the current, broad study normative consensus is assumed.

The foresight study has a mixed approach, involving both products and processes. The clients want a report containing the results of the study. However, they also want active communication of results to the appropriate target groups.

Target groups

The main target groups for this foresight study are policy-makers at VWS and healthcare inspectors at IGZ. To maximise outputs, such as learning and updating mental models, these target groups should be actively involved in the studies methods. One of the study objectives is the active communication of the results to appropriate target groups. Target groups that can benefit from information on current and expected nanomedical devices, development trends, associated risks and potential benefits are:

- Clinicians, for better patient care,
- Hospital managers, to anticipate changes in healthcare,
- Health insurers, to anticipate changes in healthcare,
- Medical device companies, to gain information on competitors and potential market directions,
- Notified bodies, to prepare and improve their risk assessments,
- European policy-makers, to incorporate expected developments in the new medical device regulation.

Study objectives

- Provide an overview of nanomedical devices currently on the market or expected within 5 years;
- Determine if trends exist for specific categories of nanomedical devices;
- Identify nano-related opportunities and risks of the different categories of nanomedical devices;
- Actively communicate relevant findings to the appropriate target groups;

The objective "Identify the most important gaps in scientific knowledge to make a good benefit-risk assessments" is dropped as this is covered by the recently published SCENIHR opinion[110]. The current foresight study will not add additional value to the information and statements made in the SCENIHR opinion (see feasibility assessment).

Outputs

- An internal report to VWS and IGZ containing:
    - An overview of nanomedical devices currently on the market (per nanomedical device category, non-exhaustive, worldwide);
    - An overview of nanomedical devices that are expected to enter the market within 5 years, (per nanomedical device category, worldwide);
    - Healthcare related opportunities and risks per product type or category of both current and expected devices;
    - An overview of general trends that can be identified for specific categories of nanomedical devices, with a statement on their opportunities and risks related to healthcare.
- Results circulating within networks of relevant target groups (informal)

Additional outputs should be discussed with the client.

Time Horizon

The time horizon is set at 5 years due to the subject being a dynamic and unpredictable technological field.

Resources

The available resources for this foresight study are € 75,000, a timeframe of 1 year and a project team consisting of four RIVM employees (2 high fare, 2 middle fare). There is support for the project within the RIVM and from the sponsoring organisations. When necessary, Adrienne Sips (who works at RIVM and has a leading role within the NanoNextNL consortium) might be asked to approach specific actors through her network. She leads the current safe-by-design RIVM project, which might be linked with the current foresight study, for example via a joint activity.

The project team has experience with desk studies and expert knowledge concerning the subject of the foresight study. Certain departments within the RIVM have experience with quantitative trend extrapolation and modelling. Furthermore, the library department can be used to conduct literature searches and modest bibliography approaches. However, this is likely not necessary as the project team has sufficient experience with scientific literature. The project team has limited experience with organising creative and interactive methods.

12.4. Method selection and framework

Information from feasibility and scoping is used to determine which characteristics are important for method selection (see chapter 9).

- Method families
  - Descriptive and matrices, Expert opinion, Monitoring and intelligence, Scenarios, and Trend analyses.
- Method characteristics
  - The aim is a mix of interaction, evidence, and expertise based methods.
  - Exploratory methods are necessary. Normative methods are unnecessary as normative consensus concerning nanomedical devices is assumed. Furthermore, predictive methods are not preferred in a rapidly changing technological field.
- Kind of data
  - The method framework will contain methods focused mostly on semi-quantitative or qualitative data, as quantitative methods are often not applicable in a rapidly changing technological field.
- Suitability for visualisation of results
  - Visualisation of results is not a priority
- Method useful in uncertain environment
  - The method framework should include methods that are useful in an uncertain environment, as technological developments within nanomedical devices are uncertain.
- Method useful in complex environment
  - Methods can be useful for both complex and non-complex environments.
- Level of interaction between participants

    - The method framework should also include one or more methods that have a high to very high interaction between participants.
- Level of experience/skill needed to perform the method
    - When the appropriate experience is not available within the project team it will be recruited elsewhere within the RIVM. Therefore, the level of experience/skill is not taken into account when selecting methods.
- Recommended time horizon
    - 5 years (short time horizon)
- Costs
    - The total framework should not cost more than € 75,000.
- Time in months
    - 12 months are available to conduct the foresight study.
- Personnel usage
    - 1-4 employees are available to conduct the methods.

Potential methods suggested according to the developed Excel-tool (filter on kind of data, method function, exploratory, time, personnel usage, and method function):

> Brainstorming, Café Seminar, Causal layered analysis, Focus group, Future workshop, Future search conference, Futures wheel, Grenelle dialogue, Identifying drivers and perspectives, Interview meeting, Interviews, Literature assessment, Meta-analysis, Morphological analysis, Perspective workshop, Polling, Relevance trees, Stakeholder panel, STEEPV (or PESTEL), Structural analysis (MICMAC method), Surveys, SWOT analysis, Web alerts.

Database searches are added to this list as additional method to find quantitative, but mostly qualitative information on marketed nanomedical devices. The Excel-tool excluded databases as a method as it is classed as quantitative. However, there are several databases that include currently available nanomedical devices (e.g. United States Food and Drug Administration 510(k) database, Health Canada Active Licence database) and databases that provide information on potential future nanomedical devices (e.g. Clinical trials.gov). Keep in mind that the Excel-tool provides suggestions, but that own experience and knowledge can often add additional possibilities.

From the list of suggestions several methods are selected based on if they can be implemented and on how they relate to the foresight studies' objectives. For example the Meta-analysis method requires several previous foresight studies concerning the chosen subject. However, feasibility assessment established that there were a very limited number of foresight studies regarding nanomedical devices. Another example is the Causal Layered Analysis, which can be used when examining the worldview and underlying emotions towards a particular technological development. However, as this is not one of the current study objectives, this method is not selected. The selected methods and their use are listed in table 7.

Table 7. Selected methods and their goal

Method	Goal
Literature review	Use scientific and grey literature to gain an overview of current and potential future products, and their opportunities and risks.
Database searches	Use databases to identify products currently on the market or use clinical trial databases to identify potential future products. This mostly concerns the qualitative data found in the databases.
Internet searches	Internet searches for currently marketed nanomedical devices.
Contact notified bodies, industry associations and medical specialty organisations	Contact the different organisations to ask for any available information on current and future nanomedical devices, and general trends.
RIVM expertise on risks	Use available expertise at the RIVM to judge potential risks for each category of nanomedical devices.
Interactive Future workshop/Café Seminar	Bring together a mix of stakeholders to gain additional input on opportunities and risks, and on future developments and general trends. Present the results from the desk study.

The interactive Future Workshop/Café Seminar provides the interactive and creative elements that are not present in the other methods. Furthermore, it can fulfil the objective of actively communicating the relevant findings to appropriate target groups. In addition, such a workshop provides a way to add additional information to the findings of the desk-based methods. It might be especially useful to identify specific trends, opportunities and risks related to the different categories of nanomedical devices. The outcomes are distributed in relevant networks as a separate workshop proceedings, and the results are used in the final report for the clients, complementing the desk-study. Potential participants for this workshop could be selected from relevant target groups and other stakeholders. The format of the workshop should be discussed with the client. Additionally, it is advised to consult RIVM foresight practitioners that have experience with these kinds of methods.

From these methods the following framework can be constructed (see figure 15). The literature review and databases are used to construct a report. This is supplemented by internet searches according to findings in the literature or databases. Relevant notified bodies (those that have nanotechnology accreditation) are contacted via phone or email to assess their opinion on general trends regarding nanomedical devices. As these notified bodies perform the assessment of class II and III medical devices containing nanotechnology their combined knowledge should help in gaining an overview of currently marketed products. This is supplemented with any information from industry or medical specialty organisations regarding current and future products. The data from all these sources is gathered in a report and used as input for an interactive workshop to gather additional information and disseminate the results. Alternative options for active dissemination are presentations at (inter)national conferences or other events. At these conferences the present experts can be used to actively gather additional information on current and potential future products, general trends, risks and opportunities.

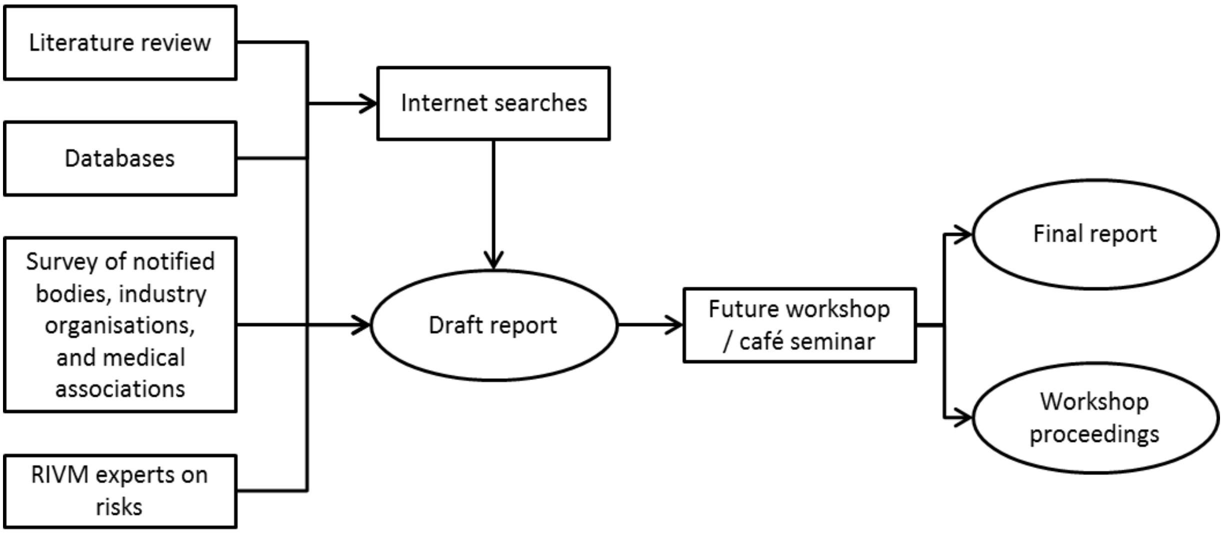

Figure 15. Nanomedical devices – Current products, future trends, opportunities and risks.

12.5. Using the checklist document to design a foresight study - afterthoughts

This foresight study was designed by the author according to the checklist document from Part 2. The design of a foresight study is an iterative process, and therefore the foresight study on nanomedical devices designed in the previous sections should be seen as a starting point for further discussion. Although assessing feasibility, scoping and selecting methods can be done by one person, as shown above, the process would be more accurate and complete when performed in a group together with the clients. Another option is to do the feasibility assessment and scoping with the project team and afterwards discuss the results with the clients to remove uncertainties and add additional information. In the end it requires time, continued communication and shared decision-making with the client and potential additional stakeholders.

The checklist document and the Excel-tool still require the foresight practitioner to do a lot him/herself. The document is not a decision-making tool, but instead it forces you to consider your project and chart the available options and context. The Excel-tool provides suggestions for methods to use, but has its limitations due to the variability of methods. The tool should therefore be combined with your own knowledge about the subject and available sources of information. By going through the methods from the start you can gain an idea of available options and use certain methods during feasibility assessment and scoping. For some methods the Excel-tool provides additional reading when required. Furthermore, reading papers or reports on foresight studies in general might provide the additional background information to design the right study for the project at hand (see appendix 3 for a list of relevant articles on foresight studies).

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Appendix

Appendix 1: Questionnaire among RIVM foresight practitioners

13 project leaders were sent a questionnaire in Dutch via email containing eight statements and three open questions. The number of questions was kept to a minimum to make sure it took the participants little time to answer the questions, thereby increasing the number of replies. The statements were all formulated in a positive way. Although the number of participants is low, the study is still useful. As all of them are actively engaged with the subject at hand, the questionnaire can be seen as a small qualitative study. The results are discussed in Part 1 of this report.

Statements (agree/disagree):

- It was clear to me how to design the foresight study. (Het was mij duidelijk hoe ik de toekomstverkenning moest ontwerpen.)
- I had no difficulties in selecting methods for the foresight study. (Ik had geen moeite met het kiezen van methoden voor het doen van de toekomstverkenning.)
- I would have liked to have had a guidance document to help me design the foresight study. (Ik had graag een leidraad gehad om mij te helpen met het ontwerpen van de toekomstverkenning.)
- I think a guidance document for designing foresight studies will add to the quality of RIVM foresight studies. (Ik denk dat een leidraad voor het ontwerpen van toekomstverkenningen kan bijdragen aan de kwaliteit van toekomstverkenningen binnen het RIVM.)
- I sought council with other foresight practitioners within the RIVM for designing my foresight study. (Ik heb advies gezocht bij andere toekomstverkenners binnen het RIVM voor het opzetten van de toekomstverkenning.)
- Other foresight practitioners are easy to find within the RIVM. (Andere toekomstverkenners zijn gemakkelijk te vinden binnen het RIVM.)
- Knowledge on foresight studies is shared within the RIVM. (Kennis over toekomstverkennen wordt binnen het RIVM gedeeld.)
- An internal knowledge network of RIVM foresight practitioners is desired. (Een intern kennisnetwerk van RIVM toekomstverkenners is gewenst.)

Open questions (translated into English):

- In which foresight studies are/were you involved?
- How did you select the methods used in your foresight study?
- How can foresight studies be further improved at the RIVM?
- Additional comments

Table A.1 Questionnaire results

Statements	Agree	Disagree	Blank
1. It was clear to me how to design the foresight study.	8	5	0
2. I had no difficulties in selecting methods for the foresight study.	7	6	0
3. I would have liked to have had a guidance document to help me design the foresight study.	8	3	2
4. I think a guidance document for designing foresight studies will add to the quality of RIVM foresight studies.	11	1	1
5. I sought council with other foresight practitioners within the RIVM for designing my foresight study.	6	6	1
6. Other foresight practitioners are easy to find within the RIVM.	4	6	3
7. Knowledge on foresight studies is shared within the RIVM.	4	7	2
8. An internal knowledge network of RIVM foresight practitioners is desired.	12	0	1

Appendix 2: List of foresight studies and practitioners at the RIVM (non-exhaustive)

Table A.2. Foresight studies conducted at the RIVM (2014 – 2015, non-exhaustive)

Project	Project leader	Department RIVM (Dutch)	Sponsor(s)	Objectives	Methods
3D printing[50] (finished 2014)	Jeroen Devilee	Milieukwaliteit en Gezondheid – Centrum Duurzaamheid, Milieu en Gezondheid	RIVM	- Identify developers and users of 3D printing - Overview of current knowledge on developments and applications - Identification of conditions required for application development - Map normative principles and visions of developers and users	Search of scientific and grey literature, Semi-structured expert and user interviews,
Capacity building Foodture (Foresight in Food)	Jeanne van Loon	Verkenningen Volksgezondheid – Centrum Gezondheid en Maatschappij		- Identification of drivers of current and future supply and consumption of food - Create and evaluate relevant societal visions from the perspective of health, safety, sustainability and the future of food - Enlarge knowledge and expertise of RIVM staff members in Foresight studies and food	Workshops for scenario building and evaluation (serie), desk research, meta-analysis of previous foresight reports
Demand coverage Dutch drinking water supply 2015-2040 (finished 2014)[54]	B.H. Tangena	Duurzaamheid Drinkwater en Bodem – Centrum Duurzaamheid, Milieu en Gezondheid	Ministry of Infrastructure and the Environment	- Determine future demand for drinking water in the Netherlands - Determine need and possibilities for optimisation of drinking water supply	Modelling, Trend extrapolation and analysis, surveys
Prospective study demand for drinking water 2040 and availability resources (finished 2015)[55]	N.G.F.M. van der Aa	Duurzaamheid Drinkwater en Bodem – Centrum Duurzaamheid, Milieu en Gezondheid	Ministry of Infrastructure and the Environment	- Determine is the Netherlands has sufficient drinking water capacity in 2040 - Suggest solutions for potential insufficient capacity	Grey literature, Scenarios, Trend extrapolation, Regional stakeholder workshops
Nanomedical devices – A horizon scan	Robert Geertsma	Productveiligheid – Gezondheidsbescherming	Ministry of Health, Welfare and Sport, Dutch Health Care Inspectorate	- Overview of current products and short term (5y) developments in nanomedical devices - Identification of opportunities, risks and knowledge gaps	Market reports, Literature searches

Nanomedicinal products (finished 2014)[52]	Robert Geertsma	Productveiligheid – Gezondheidsbescherming	Ministry of Health, Welfare and Sport, "Onderzoeksprogramma Geneesmiddelenketen"	- Overview of current and future (5y) products	Literature searches, Clinical trials
Nanomedicinal products – A horizon scan	Cornelle Noorlander	Consumenten en Productveiligheid – Centrum Veiligheid Stoffen en Producten	Ministry of Health, Welfare and Sport	- Overview of developments on short-midterm (5-15y) - Identification of opportunities, risks and potential impact on current policy and regulations - Possible recommended governmental actions	Literature searches, Clinical trials, Meta-analysis of Foresight Studies performed by other organisations
New medical technologies (finished 2015)[53]	Claudette de Vries	Product safety – Centre for Health Protection	Dutch Health Care Inspectorate	- Identify future medical technologies and associated risks	Scientific literature, Clinical trials, Expert interviews, Questionnaire ~100 hospitals
Personalised medicine	Marjolein Weda	Effects on Public Health – Centre for Health Protection	Ministry of Health, Welfare and Sport	- Overview of current use of personalised medicine - Identification of current barriers and drivers - Identification of most important policy themes and their prioritisation - Future products of personalised medicine (5-10y), their risks and opportunities - Future perspective of the use of personalised medicine, identification of barriers - Policy recommendations regarding future of personalised medicine	Scientific and grey literature, Expert interviews
Public Health Status and Foresight Report 2014 (finished 2014)[29]	Jeanne van Loon	Verkenningen Volksgezondheid – Centrum Gezondheid en Maatschappij	Ministry of Health, Welfare and Sport	- Overview of disease, health, health-influencing factors, healthcare and related policy in the Netherlands - Develop normative scenario's to improve understanding and discussion of Dutch healthcare	Scenario building with stakeholders and experts, Trend extrapolation and analysis, Modelling, Literature searches, Databases, Delphi-like method (TNO Group decision support system)

Sport Foresight study	Marieke van Bakel	Verkenningen Volksgezondheid – Centrum Gezondheid en Maatschappij	Ministry of Health, Welfare and Sport	- Foresight on the future of sport in the Netherlands	To be determined
Synthetic Biology	Jaco Westra	Gentechnologie en Biologische Veiligheid – Centrum Veiligheid Stoffen en Producten	Ministry of Infrastructure and the Environment	To be determined	To be determined
Technology exploration National Security (finished 2014)[56]	Leendert Gooijer	Integrale Ruimtelijke Vraagstukken – Centrum Duurzaamheid, Milieu en Gezondheid	Ministry of Safety and Justice	- Gain broad insight on technological developments and their associated opportunities and threats to national security	Interviews, Literature study, Expert panels, Megatrends,

Appendix 3: Checklist for designing foresight studies – a compact working version

1. Introduction

Goal. The goal of this document is to assist RIVM foresight practitioners in designing a foresight study. This document provides the foresight practitioner with a checklist to make sure essential steps are not skipped. It is not a guideline that makes choices for you, but it forces you to make choices yourself. After following this document, and with the help of the developed Excel-tool, the foresight practitioner should be able to select appropriate methods and construct a method framework to conduct the foresight study.

Target audience. The target audience consists of foresight practitioners, both at the RIVM and beyond. This document can assist in the design of any foresight study, no matter the subject or scope. Inexperienced foresight practitioners will benefit most from this document. However, experienced practitioners can still benefit from this checklist and gather inspiration for new methods.

Outline. This document covers the three interconnected phases (feasibility assessment, project scoping, and method selection) that make up foresight study design. These phases are performed simultaneously and iteratively, together with the client and/or key stakeholders. Making decisions in one phase will affect decisions in the others phases. Figure A.1 provides an overview of the three design phases.

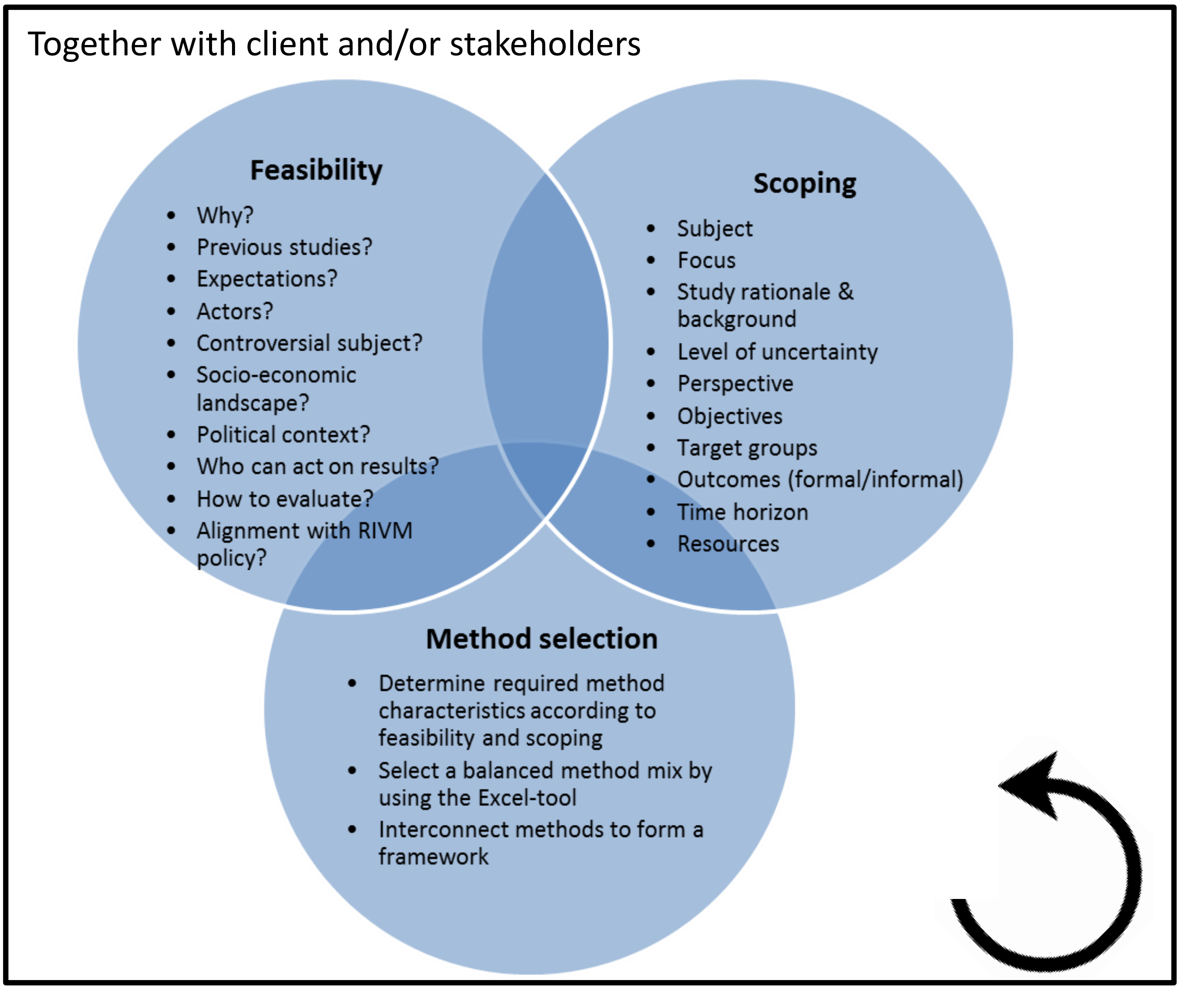

Figure A.1. The three overlapping phases of foresight study design.

Sources. This checklist document is based on the works of several authors (see references). A number of large guidelines have been made over the years and this checklist document aims to capture the most significant steps in the design process of foresight studies by comparing the different references. These written sources are supplemented by external consultation with two foresight experts, namely Ellen Willemse (Netherlands Study Centre for Technology Trends, STT) and Dr. P.A. van der Duin (Assistant professor Delft University of Technology). A comprehensive version of the checklist document and an example (foresight study on nanomedical devices) can be found in the internship report: Foresight Studies at the Centre for Health Protection – A checklist document for foresight studies, R. van der Stijl, 2015.

2. Assessing feasibility

The goal of assessing feasibility is to determine whether the foresight study can obtain satisfactory results given the study's context, before committing substantial resources. Assessing feasibility forces you to make assumptions explicit. This is done by answering a number of questions. These questions force you to think about the intended study and its surrounding forces. The answers will provide you and your client with a clearer picture of the project.

It is possible that some of the questions below are not applicable to your specific foresight study or that some questions cannot be answered until after scoping and method selection is complete.

Discuss these questions and answers with the project's clients and/or important stakeholders, as after feasibility assessment the project team and the client should decide whether to proceed, refocus, or cancel the foresight study.

Why

It is important to determine why you are conducting the foresight study, how it is different from already present exercises and how it will add extra value to the client and other stakeholders. Perhaps previous studies already provide the necessary answers the client is looking for.

Q: Why are we conducting a foresight study?

- *What is the added value of the foresight study?*
- *Is the subject still relevant in the future?*
- *What activities or studies on the same subject are already done or on-going?*
    - *Can I make use of these studies?*
    - *How can I differentiate from these studies or add additional value?*

Who

Communicating with the client about his/her expectations during and after the study will help in getting everyone on level terms and give direction to the project.

Q: Who is the main client or sponsor of the foresight study?

- *What are the expectations of the client towards the foresight exercise?*
- *How will the client use the results of the foresight study?*

It is recommended to determine as many actors as possible related to the subject of the foresight study and chart their importance and relationships (example of a tool for stakeholder analysis http://www.csu.edu.au/__data/assets/pdf_file/0018/109602/EFS_Journal_vol_5_no_2_02_Kennon_et_al.pdf). Actors can be organisations and individuals. Consider involving important actors in the foresight study. The overview of actors can later be used to find participants for foresight methods.

Q: Who are the main actors related to the subject of the foresight study?

- *What position does each actor take?*
- *Are there key stakeholders that should be involved in the study?*
- *Which actors are under your control or influence, and which are not?*
- *Which actors can help the foresight study? Which actors might oppose it?*
- *Are there initiatives or agendas that could influence the foresight study, in scoping, or need for timing or cooperation?*
- *Which of the actors is in a position to act on the result of the foresight study?*
- *Who are potential ambassadors (important supporters) and should they be approached?*
- *Is there enough support for the foresight study?*
- *Which actors might be (in)directly affected by the results of the foresight study?*

What

Foresight studies are always embedded in a subject-dependent political, economic, and cultural context. This context can have a large influence on the success, direction, and objectives of the foresight study, and should therefore be analysed beforehand. For example, in a context marked by conflict between actors the objective might be to map the normative values of each actor, develop mutual understanding and start a conversation.

Q: What kind of techno and socio-economic landscape surrounds the subject?

- *What are the current Political, Economic, Social, Technological, Environmental, Legal (PESTEL) factors surrounding the subject?*
- *Is the subject's landscape characterised by conflict or complacency?*
- *Is there a culture of collaboration?*
- *What is the general attitude of the landscape towards foresight studies?*
- *Is the subject of the foresight study potentially controversial?*
    - *How am I going to deal with a controversial subject?*

If the subject has a strong political aspect, give extra attention to the political context. When aiming for policy advice or action the foresight study has to be in harmony with the policy-making process in terms of timing, cultural compatibility and usability. Involving political decision makers or policy-makers can ensure that the foresight studies' results are acted upon. Working together will build mutual trust, but their involvement should not jeopardise the studies' creativity and independence.

Q: What is the political context of the foresight study?

- *Who are the main political actors with regards to the subject?*
- *What is the political culture surrounding the subject?*
- *What is the position of the foresight study in the policy cycle?*
    - *Is the subject already on the policy agenda?*
- *Is the political environment stable or instable?*
- *Can the study link up with already on-going activities or agendas?*
- *Can policy-makers be directly involved in the design or execution of the foresight study?*
- *Is the foresight study aiming for a certain policy implementation?*
- *How will you generate policy support for the foresight study?*

Goals

State the results the foresight study should achieve, and when you and the client will be satisfied with these results. Making this explicit helps in evaluating the study afterwards.

Q: What do you want to achieve with the foresight study?

- *When are you and the client satisfied with the results?*
- *What are the measureable outcomes?*
- *When do you achieve your results?*
- *How are you going to evaluate the foresight study?*
- *Are there enough resources to conduct the foresight study and gain valuable results?*
- *Are the necessary capabilities available to conduct the foresight study?*

RIVM policy

By aligning your foresight study to RIVM corporate policy and subject-related policies the foresight study becomes more relevant for the RIVM.

Q: How do we align the study with RIVM policy?

- *Are there additional RIVM policies or strategies influencing this foresight study?*
- *How do we connect to society with this foresight study?*
- *How do we capture and secure relations?*
- *Are we going to collaborate with internal or external multidisciplinary parties?*
- *How are we going to be more proactive and show guts?*

3. Scoping

During the scoping phase, the project team, the client and/or relevant key stakeholders decide upon the parameters that determine the form and scope of the foresight study. Scoping involves gathering background information; collecting views and advice on the study from other foresight practitioners; and discussing different project blueprints with the client and/or other stakeholders.

The product of this phase will be a blueprint of the foresight study in which decisions are made explicit. This blueprint will affect the selection of methods and the method framework. The following scoping parameters are important to consider:

Focus: Focus is on a specific issue, geographical territory, sector, or on a combination of these factors. The level of required detail (e.g. broad, narrow) should be made explicit.

Stable vs. unstable future: Is the future continuous or unpredictable and dynamic? Quantitative methods have less predictive power in unpredictable futures.

Perspective: The adopted perspective should match objectives and outcomes. Examples of perspectives are scientific, technological, institutional, social or economic perspectives.

Type of uncertainty: What uncertainties are present regarding your subject? Are there only cognitive uncertainties or also social and normative uncertainties? This influences the studies objectives and choice of methods.

Top-down vs. bottom-up: Will there be emphasis on interaction?

Product vs. process: What tangible and intangible outcomes do you focus on? What has priority?

Target groups: Target groups consist of direct users and indirect users affected by the study. An overview of relevant target groups helps in decision-making and results dissemination.

Objectives: A foresight study can have multiple main and side objectives. The objectives need to be carefully defined, clear and unambiguous from the start of the foresight study. The goal is to create a clear understanding of the objectives among the client, sponsors, project coordinator and the implementing staff. The objectives should be realistic in relation to the available money and time. If there are multiple objectives it should be clear on which emphasis is placed, as this will influence the choice of methods.

Outputs: Translate the objectives into more specific outputs that the foresight study should produce. Outputs that are not stated beforehand will not be addressed adequately later on. Outputs can be either tangible (e.g. reports, x workshops, websites) or intangible (networking activities, updated mental models, new knowledge).

Time horizon: Common sense and pragmatism should guide the selection of an appropriate time horizon. Different time horizons are suitable for different methods. The time horizon depends largely on the subject and the associated sector. Fast changing and dynamic subjects require a short time horizon.

Resources: List the available resources to conduct the foresight study, including financial resources, time, (political) support, human resources and RIVM resources. Discuss these resources with the client.

4. Method selection

The goal is to select a balanced mix of methods to build a method framework that fits the purpose of the foresight study. Address potential pitfalls and risks in your design. Weaknesses of one method should be offset by another method. Ultimately, consult with the client and/or key stakeholders on the selection of appropriate methods and the framework.

It is difficult to provide simple guidelines for selecting and combining methods, as most methods can be used in multiple ways and for multiple goals. A foresight study often consists of an orientation or diagnosis phase that investigates the status quo; a prognosis phase where forward-looking methods are employed; and a prescription phase where decisions and future actions are determined. The selection of methods depends upon the criteria determined during the feasibility assessment and scoping phases. The most important criteria are study objectives, available time, financial resources, desired outputs, prevalent uncertainties, and time horizon.

Excel-tool for selecting foresight methods

The developed Excel-tool allows for the selection of methods based on the decisions and considerations made during feasibility assessment and project scoping. The Excel-tool contains 63 methods and tools, of which the following characteristics are described or scored:

- General description of the method
- Advantages and disadvantages
- General comments
- Potential output
- Objective families
    - Cooperation and networking, Policy development, Barriers and drivers of science, technology and innovation (STI), Future thinking, STI strategy/priority-setting, Research/investment areas, Shared visions, Grand Challenges, Actions and discussions
- Method families
    - Creativity, Descriptive and matrices, Statistical, Expert opinion, Monitoring and intelligence, Modelling and simulation, Scenarios, Trend analyses, valuing/decision/economic

- Method characteristics
    - Creativity, interaction, evidence, expertise
    - Predictive, exploratory or normative
- Method function
    - Diagnosis, prognosis, prescription
- Kind of data
    - Quantitative, semi-quantitative, qualitative
- Suitability for visualisation of results
- Suitability for combining with other methods
- Method useful in uncertain environment
- Method useful in complex environment
- Level of interaction between participants
- Level of experience/skill needed to perform the method
- Experience available at the RIVM
- Recommended time horizon
- Costs
- Time in months
- Personnel usage
- Recommended additional reading

The Excel-tool allows you to filter methods based on the abovementioned characteristics (see figure A.2).

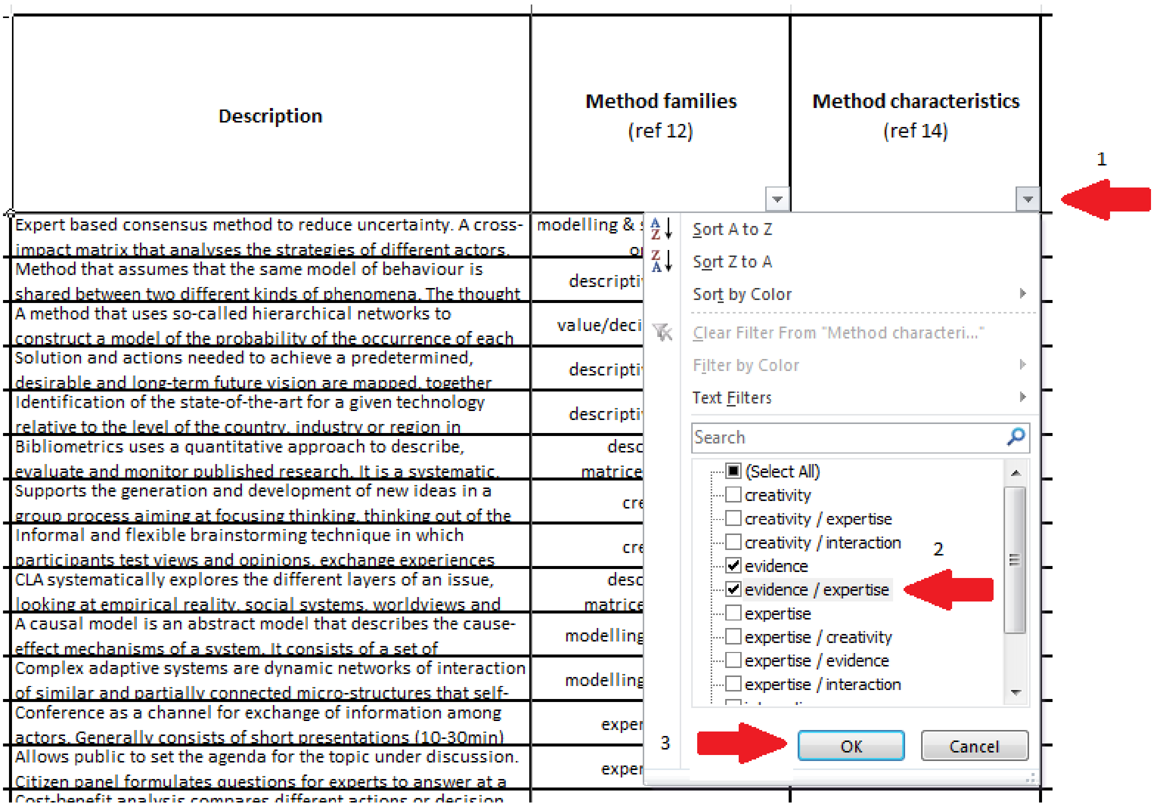

Figure A.2. How to use the Excel-tool. 1) Click the arrow to open the filter options. 2) Select which characteristics should be included (ticked box) or excluded (blank box). 3) Click OK to filter methods based on selected characteristics. It is possible to set multiple filters simultaneously. To remove filters, open filter options and choose “select all”. Do not forget to select “blank” as a filter option to include methods that do not fit one specific input.

Be aware that the Excel-tool does not list all available foresight methods, nor does it claim to be correct on all fronts. Most methods employed in foresight studies are highly flexible. Therefore, the assigned characteristics and descriptions can change depending on the study circumstances. The methods shown by the Excel-tool are suggestions only. In the end, it is up to the project team, in consultation with the client and/or stakeholders, to select which methods to use.

Building a method framework
Selected methods are combined to form a framework where one or more methods serve as input for others, ultimately resulting in the desired outputs. The goal of the framework is to interconnect methods to gain an interdisciplinary foresight study design. Figure A.3 shows an example of a method framework from two subsequent RIVM foresight studies on drinking water. Additional examples can be found in the internship report.

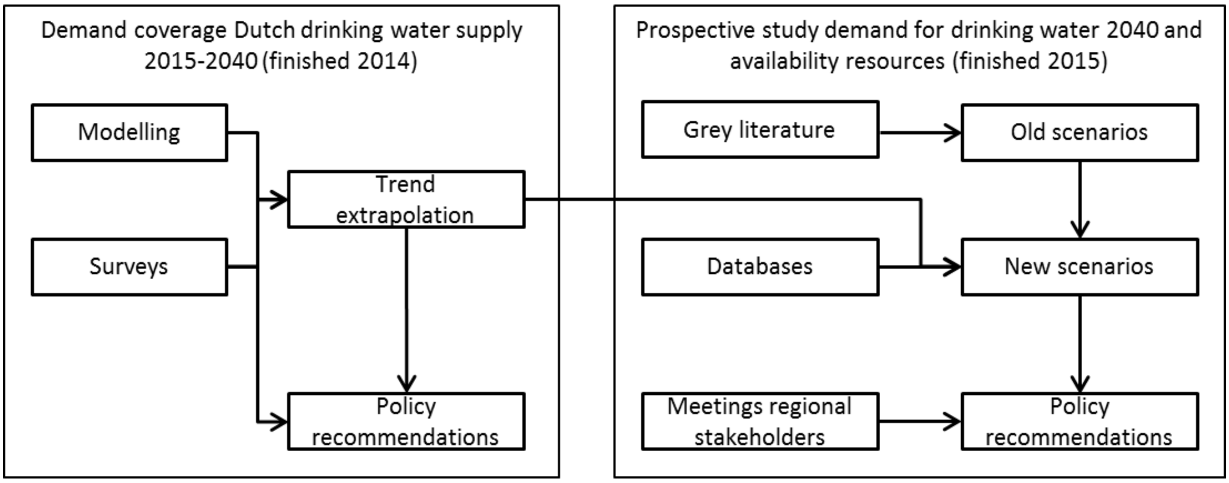

Figure A.3. Framework for Dutch drinking water supply 2015-2040 combining two foresight studies. Left study: 1) Modelling of current and future drinking water supply. 2) Use model and drink water company surveys to extrapolate future trends. 3) Form policy recommendations using the demand forecast and available capacity. Right study: 1) Use literature to orientate on Dutch province policy regarding drinking water extraction. 2) Use old scenarios, updated by new information from databases, and extrapolated trends from study 1 to form min, trend, and max scenarios. 3) Make policy recommendations based on scenarios and meetings with regional stakeholders.

5. Take home messages

- Collaborate with the client and when necessary key stakeholders to design a foresight study that attempts to fit everyone’s needs and wishes.
- Designing a foresight study is an iterative process that requires multiple rounds of open communication between the different parties.
- Choose a well-balanced mix of methods.
- Avoid the pitfall of technological determinism. Technology is eventually used by society and therefore societal and normative aspects can play a large role in the future of technological innovations.

- The Excel-tool offers suggestions for methods to use. Due to the complexity and variation of foresight studies and the versatility of many methods you should feel free to deviate from the Excel-tool according to your own insights.

- Foresight studies are not the exclusive terrain of foresight experts. Foresight practitioners from all skill levels are encouraged to conduct foresight studies, as practise is the best way to learn about foresight

Appendix 4: Relevant literature related to foresight studies

Table A.3. Relevant foresight literature

Literature	Description
A toolkit for the identification and assessment of new and emerging health technologies EuroScan International Network, 2014	The main stages involved in early awareness and alert (EAA) systems continue to be: identification of information on new and emerging technologies (horizon scanning); filtration and prioritisation of the identified information; and assessment of the technology or group of technologies. The toolkit provides guidance on these stages and highlights the various approaches that can be taken at each of these stages depending on the context of the EAA system and resources available.
Een praktische handleiding voor regionale toekomstverkenning in Nederland Europese Commissie, Directoraat-generaal Onderzoek	Handleiding voor regionale toekomstverkenningen opgesteld door de Europese Unie gericht op toekomstverkenners en gebruikers van toekomstverkenningen. Uitleg hoe regionale toekomstverkenningen in de praktijk kunnen worden gebracht.
Leidraad Stakeholderparticipatie voor het Milieu- en Natuurplanbureau: Praktijkwijzer Planbureau voor de Leefomgeving, 2007	De Leidraad Stakeholderparticipatie is bedoeld om projectleiders van het Milieu- en Natuurplanbureau (MNP) bij het maken van keuzes voor participatie te ondersteunen en te begeleiden. Deze praktijkwijzer van de Leidraad Stakeholderparticipatie bevat informatie over de volgende onderwerpen: stakeholderselectie; methodenselectie; interactieve workshops; participatiemethoden; en praktische tips voor participatieve projecten.
Participatory Methods Toolkit – A practitioner's manual King Baudouin Foundation and the Flemish Institute for Science and Technology Assessment (viWTA), 2005	Practical guidelines or approaches for starting and managing participatory processes. This publication is meant to be a working tool. The document contains an in-depth description of 13 methods, complemented with a short description of 36 additional participatory methods.
Scenario's maken voor milieu, natuur en ruimte: een handreiking Planbureau voor de Leefomgeving, 2013	Het Planbureau voor de Leefomgeving heeft op basis van jarenlange ervaring met het maken van toekomstscenario's een handreiking geschreven. Deze handreiking geeft een overzicht van de belangrijkste stappen die in een scenariostudie kunnen worden gezet, de keuzes die hierbij kunnen worden gemaakt en de mogelijkheden en beperkingen die de keuzes met zich meebrengen. De handreiking is bedoeld voor medewerkers van planbureaus en andere onderzoeksinstellingen, maar kan ook waardevol zijn voor opdrachtgevers van scenariostudies.

Scanning for early recognition of emerging issues; dealing with the Unexpected – An operational framework for the identification and assessment of new future developments SESTI Methodology Workshop 26 October 2010	The SESTI project focuses on the new foresight approaches that can be used to identify “weak signals” and emerging issues in a systematic, efficient and effective way, it pursues their operationalisation by linking them in a meaningful way to policy processes.
Toekomstonderzoek voor organisaties Patrick van der Duin, 2012	Dit handboek helpt organisaties toekomstonderzoek te doen en toe te passen in een besluitvormings-proces. Ook kunnen ze met dit boek beoordelen of uitbesteed toekomstonderzoek een goede kwaliteit heeft en nuttig is om te gebruiken. Het boek beschrijft verschillende methoden en technieken voor het doen van toekomstverkenningen.
Uit zicht – toekomstverkennen met beleid Wetenschappelijke Raad voor het Regeringsbeleid, 2010	Toekomstgericht beleid vereist het anticiperen op mogelijke, doch onzekere ontwikkelingen. Het nadenken over de lange termijn kan in beleid en politiek op verschillende manieren vorm krijgen. Toekomstverkenning is een manier om dat systematisch te doen. Maar wat geldt als goed toekomstverkennen? In de bundel Uit zicht: toekomstverkennen met beleid wordt een actueel begrippenkader uiteengezet om kritisch op toekomstverkenning te kunnen reflecteren en worden valkuilen en uitdagingen inzichtelijk gemaakt.
UNIDO Technology Foresight Manual – Organization and methods (volume 1) United Nations Industrial Development Organization, 2005	The manual is mainly based on papers presented at a series of events organized by UNIDO as part of this regional initiative. Module 1 Introduction to Technology Foresight Module 2 Organizing a Technology Foresight Exercise Module 3 Technology Foresight methods
UNIDO Technology Foresight Manual – Technology Foresight in Action (volume 2) United Nations Industrial Development Organization, 2005	Module 4 Technology Foresight at the National Level Module 5 Technology Foresight at the Supranational Level Module 6 Technology Foresight at the Subnational Regional Level Module 7 Technology Foresight at the Company Level

Websites on foresight studies:

- European Foresight Platform (http://www.foresight-platform.eu/)
- FOR-LEARN Online Foresight Guide (http://forlearn.jrc.ec.europa.eu)
- *Doing Foresight* (http://doingforesight.org/)

Appendix 5: Abstract for the 8th Conference of the European Foundation for Clinical Nanomedicine (CLINAM), 28 June – 1 July 2015, Basel, Switzerland

human disorders. These nano-scale assemblies are predominantly rich in β-sheet secondary structure and specifically bind dyes, such as ThT and Congo-red. The formation of the amyloid fibrils or earlier pre-fibrillar forms correlates with an apoptotic effect in various tissues. While the formation of these cytotoxic supramolecular entities has previously been linked to proteins and peptides, we had later demonstrated that the single phenylalanine amino acid can also form amyloid-like fibrils possessing typical ultrastructural, biophysical and biochemical properties. Moreover, these fibrillar assemblies are cytotoxic by the induction of apoptotic programmed cell death. Physiological phenylalanine accumulation is detected in the plasma, cerebrospinal fluid and brain tissues of phenylketonuria (PKU) patients. The generation of antibodies in a PKU mice model and identification of aggregate deposits post mortem in patient brains suggested a pathological role for these assemblies. Thus, the formation of tangled amyloid-like fibrils by phenylalanine may propose a new amyloidal etiology for PKU. Furthermore, these findings may offer that materials known to inhibit amyloid structure formation may also inhibit other amyloid-like structures and thus, may lead to new innovative direction of treatments for PKU patients, which suffer from profound and permanent mental retardation.

NANOTECHNOLOGY IN MEDICAL DEVICES: HORIZON SCAN, RISK ASSESSMENT AND REGULATORY DEVELOPMENTS

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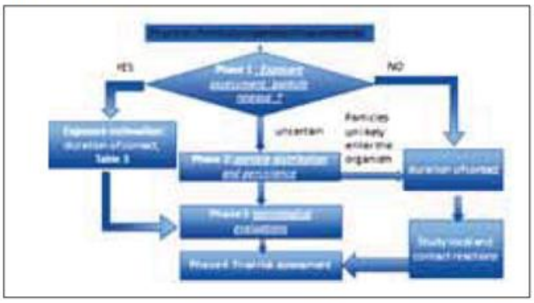
Innovative nanotechnologies are increasingly used in medical applications and are expected to have a major impact on healthcare in the future. These nanotechnology enabled medical innovations relate to both medicinal products and medical devices. In this study we have focused on medical devices.

Nanotechnology applications in the field of medical devices, also referred to as "nanomedical devices", span a wide range of very diverse products, technologies and application areas. Their intended use can be in the context of therapy, diagnosis, monitoring and/or prevention of disease. All medical disciplines are benefiting from nanomedical devices, especially orthopaedics, dentistry, oncology, and cardiology. Also a number of innovations in clinical chemistry laboratories are enabled by nanotechnologies. Nanomedical devices can involve the use of nanomaterials, however, nanotechnologies also enable innovative devices without using nanomaterials, for example by applying nano-electronics or lab-on-a-chip technologies. The use of nanomaterials in medical devices poses a particular challenge for the safety evaluation and risk assessment of these medical devices as the specific character of the nanomaterial used should be taken into consideration. Nanomedical devices can be non-invasive or invasive, resulting in potential contact with any kind of tissue. It is important to have clear insights into the state of affairs with regard to the availability of nanomedical devices and their specific benefits and risks, not only for regulators and industry, but also for physicians and pharmacists.

In the present study, we have carried out a horizon scan to identify nanomedical devices that are currently available on the market or under evaluation in clinical studies. In addition, we have analyzed the most promising research developments, potentially leading to products in the future. A variety of data sources was explored, including a search of scientific literature and clinical trial registries, analysis of databases from FDA and Health Canada, patent analysis and commercial market reports.

Furthermore, the various aspects of safety evaluation and risk assessment of medical devices containing nanomaterials were addressed, based on the Scientific Opinion "Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices", published in January 2015 by the European Commission's Scientific Committee on Newly Identified Health Risks (SCENIHR). SCENIHR recommends a phased approach for evaluating the risk of the use of nanomaterials in medical devices based on potential release and characteristics of the nanomaterials, in order to avoid unnecessary testing. The phases cover particle release (phase 1), particle distribution and persistence (phase 2), hazard assessment (toxicological evaluations) (phase 3), risk characterisation/risk assessment (phase 4). See Figure 1 for a graphical representation of this phased approach.



Finally, an overview of current developments in regulation and standards for medical devices with relevance for the application of nanotechnologies is provided. This includes activities of the European Commission's Working Group on New and Emerging Technologies in medical Devices (NET WG) related to the ongoing revision of the regulatory framework for medical devices. Also, a guidance document is currently under development within the International Organization for Standardization (ISO), entitled "ISO/NP TR 10993-22 Biological evaluation of medical devices – Part 22: Guidance on nanomaterials".

ETHICAL ISSUES IN PATIENTS' INVOLVEMENT IN DECISIONS MAKING ON PERSONALIZED TREATMENTS WITH NANOMEDICINE/S: PROTECTION VERSUS THE FRONTIERS OF HOPE

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Nanomedicine, in an ever increasing manner and speed, becomes a constitutive part of the new medicine of the 21st century. It permeates all its disciplines with new, revolutionary materials, devices, nano-medicines, and never-before-encountered technological possibilities. Distinguishing between treatment 'hypes' and real hopes for cure of the most dreadful human diseases and ailments does become difficult even for a well-educated health professional. Needless to say anything about a vulnerable patient, navigating anxiously, with his or her semi-blind confidence, the vast, sometimes rather ugly and dangerous 'waters' of nowadays' Internet (dis)information. 'Pirates' of the 'profit business for all costs' are prepared, hiding well in the 'information fog', to prey with insatiable greed on his or her infinite hopes, earthly despair, and immitigable suffering; making profits without borders and leaving the exploited individual alone, when he or she has failed the expectations of alleged 'miraculous cures'. Media and politics are not providing much help either.

In contrast to this dreadful imaginary, there is a colossal effort of the real science and research, pushing the 'frontiers of possible' towards ever new horizons, while taking into account the patient, present and future, with his or her still unmet (and growing) needs; coloured with real human fears and sorrows. Seeking the informed participation of the patient as a partner and subject of their honourable, very expensive, and sometimes even risky efforts.

These complex and dynamically evolving realities provide for as yet rather poorly explored universe of the moral/ethical inquiry. It