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Brief Communication

Risk Analysis and Technology Assessment in Support of Technology Development: Putting Responsible Innovation in Practice in a Case Study for Nanotechnology

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ABSTRACT

Governments invest in "key enabling technologies," such as nanotechnology, to solve societal challenges and boost the economy. At the same time, governmental agencies demand risk reduction to prohibit any often unknown adverse effects, and industrial parties demand smart approaches to reduce uncertainties. Responsible research and innovation (RRI) is therefore a central theme in policy making. Risk analysis and technology assessment, together referred to as "RATA," can provide a basis to assess human, environmental, and societal risks of new technological developments during the various stages of technological development. This assessment can help both governmental authorities and innovative industry to move forward in a sustainable manner. Here we describe the developed procedures and products and our experiences to bring RATA in practice within a large Dutch nanotechnology consortium. This is an example of how to put responsible innovation in practice as an integrated part of a research program, how to increase awareness of RATA, and how to help technology developers perform and use RATA. *Integr Environ Assess Manag* 2018;14:9–16. © 2017 The Authors. *Integrated Environmental Assessment and Management* published by Wiley Periodicals, Inc. on behalf of Society of Environmental Toxicology & Chemistry (SETAC)

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INTRODUCTION

The speed of development and introduction of new technologies into society is dazzling. Governments worldwide invest huge sums in developing "key enabling technologies," expected to significantly contribute to solve societal challenges and boost national economies. The public sector is an important player in stimulating and financing technology development (Mazzucato 2013) and has a role to protect humans and the environment against still-uncertain possible adverse effects of new technologies.

In response, much attention is paid to responsible research and innovation (RRI) (von Schomberg 2012; Owen et al. 2012; Douglas and Stemerding 2013; Stilgoe et al. 2013; Rip 2014), including social, sustainability, ethical, and moral concerns about innovation processes. Research and innovation can be defined as "a transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (ethical) acceptability, sustainability and societal desirability of the innovation process and its marketable products in order to allow a proper embedding of scientific and technological advances in our society" (von Schomberg 2012). In line with this definition, the term "risk innovation" was proposed to match and complement technology innovation, and to promote the development of tools and practices that protect social and environmental values while enabling creation and growth (Maynard 2015).

There are numerous examples of risks that were broadly recognized only after market introduction of new products or technologies, often neglecting early warnings (EEA 2013). If there is any doubt among the public about safety aspects, acceptance and implementation of new technologies in society can be seriously hampered and thus potential benefits may not be fully realized (Gupta et al. 2013). Examples of such "contested technologies" are genetically

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modified organisms, genetic technology, fracking technologies for shale gas, biofuels, and C capture and storage (e.g., Cuppen et al. 2015; Dignum et al. 2016).

Chemical products are registered and evaluated for their possible risks to humans and the environment before market introduction. In Europe this evaluation is regulated by legislation for industrial chemicals, biocides, pesticides, (veterinary) pharmaceuticals, cosmetics, food additives, and so on.

Comparative legislation as exists for chemicals to prevent adverse human, environmental, or societal risks after market introduction has not been elaborated for technological developments in a broader sense, apart from generic legislation on product safety (2001/95/EC). However authorities, industries, investors, and insurance companies demand answers to questions concerning risks of emerging technologies and to decrease inherent risk uncertainties. Addressing such questions requires smart approaches, applicable to a broad set of technological developments, to swiftly reduce uncertainties to acceptable levels.

SOME BACKGROUND ON RESPONSIBLE RESEARCH AND INNOVATION

Responsible research and innovation received a prominent place in the European Union's (EU) policies regarding research funding and technology development. As a "cross-cutting issue," RRI is promoted throughout the EU's Horizon 2020 research program. Although definitions are available (von Schomberg 2012; Rip 2014) and RRI is even considered a buzzword (Bensaude Vincent 2014), a recent literature review shows that RRI is still loosely articulated, and further operationalization is required (Ribeiro et al. 2016). Generally RRI emphasizes consideration of ethical and social aspects of research and innovation in addition to natural sciences, and therefore asks to combine assessments from different perspectives. To this end, the TranSTEP approach was developed, which pleads for maximizing the integration of various existing assessment methodologies including, for example, technology assessment (TA), risk analysis (RA), and life cycle analysis (LCA) (Forsberg et al. 2016).

Responsible innovation received much attention in the context of developing nanotechnologies, related to concerns about possible human and environmental risks and about a possible lack of acceptance (Rip 2014; Erbis et al. 2016). Several countries therefore organized dialogues on nanotechnology (Tomellini and Giordani 2008; Krabbenborg 2012; Pfersdorf 2012).

RISK ANALYSIS AND TECHNOLOGY ASSESSMENT

Both risk analysis and technology assessment, together referred to as "RATA," have a strong and long-standing scientific basis that is well applicable in the context of responsible innovation.

Risk analysis of human and environmental health effects of chemicals has its basis in natural sciences, mainly chemistry, toxicology, ecology, and statistics (van Leeuwen and Vermeire 2007). Risk analysis is embedded in many chemical legislations and accompanying guidance documents worldwide. Risk analysis requires data on physicochemical properties, expected emissions, degradation, sorption, (eco)toxicity, kinetics, bioaccumulation, etc. Assessment factors are used to cope with uncertainties. Hazardous properties of a chemical are assessed for human and environmental health, based on toxicity tests with cell-based assays, organism or cosm studies, or quantitative structure–activity relationships or read-across approaches. Depending on the chemical structure, more attention can be paid to specific modes of toxicological action, such as genotoxicity or endocrine disruption. In addition, the exposure toward the chemical is assessed. For human exposure via consumption and use, the workplace or the environment is assessed. For the ecosystem, the exposure of species via the various compartments of soil, sediment, water, and air, and by the food chain are assessed. Exposure assessment is based on the fate of the chemical, combined with the specific emission pattern. Finally in RA, the level at which the exposure takes place is compared to the level exerting adverse effects. A tiered approach can be used, in which higher tiers are more labor and data intensive and in which measures to mitigate exposure can be included. Life cycle assessment approaches can be integrated in RA to include all impacts during the life cycle of the (nano)chemicals, that is, the production, use, and disposal phases (Grieger et al. 2012; Gilbertson et al. 2015; Walker et al. 2015; Subramanian et al. 2016).

Technology assessment assesses the possible effects and futures of a technology in society (van den Ende et al. 1998). This includes the public's perception, different stakeholders' perspectives, possible changes in responsibilities, and liabilities of and between actors. Participatory methods are therefore important for TA (Burgess and Chilvers 2006). Because social impacts are viewed as core dimensions of technological development, TA seeks to shape technology and social contexts through information, interaction, and dialogue (Fleischer and Grunwald 2008; Russell et al. 2010). Technology assessment has its basis in social sciences, mainly sociology, psychology, ethics, and philosophy. Technology assessment is not embedded in legislation, but is commonly used where consumers or the general public participate in the assessment (Frewer 1999).

Used in combination, risk analysis and technology assessment can provide a scientific basis to assess human, environmental, and societal risks of new technological developments and their applications, and thus can be considered relevant for responsible innovation. This assessment can be applied during different stages of technology development (e.g., von Gleich et al. 2008).

RISK ANALYSIS AND TECHNOLOGY ASSESSMENT AND NANONEXTNL

Here, we describe our experiences to bring RATA in practice in the context of nanotechnology development within NanoNextNL, a large-scale Dutch national research and technology program for micro- and nanotechnology (www.nanonextnl.nl). More than 100 companies, universities, knowledge institutes, and university medical centers were involved, the total sum was €250 million, and the program ran from 2010 until 2016. During the formation of NanoNextNL, political attention was paid to concerns for adverse effects of nanotechnology. The Dutch parliament requested that 15% of the total budget of NanoNextNL be granted for risk and impact research, as a precondition and accelerator for innovation. Within NanoNextNL, risk analysis and technology assessment were put together in 1 RATA theme, in addition to 9 other themes (Walhout and Konrad 2015). Five themes gained fundamental insight into nanotechnologies, while 4 themes applied nanotechnologies in the food, water, energy, and pharma sectors (Figure 1; for more information see NanoNextNL 2017).

The RATA theme was divided into 3 programs, focusing on human risks, environmental risks, and technology assessment. The aim was to create excellent science in support of regulation of nanomaterials. This was put in practice via participation by program members in the Scientific Committees of the European Commission, European Chemicals Agency (ECHA), International Organization for Standardization (ISO), Organisation for Economic Co-operation and Development (OECD), and others. Next, the ambition was to bridge innovation with safety and society requests, by facilitating interaction between RATA and the other themes.

The main topics for the human health program were detection, exposure, bioavailability, and toxicity (e.g., Marvin et al. 2013; Bekker et al. 2015; Bezantakos et al. 2015; Braakhuis et al. 2015, 2016; Kloet et al. 2015; Walczak et al. 2015). In this program, new approaches and tools are developed to describe responsible use of nanomaterials for workers and consumers, and models to prioritize nanomaterials for higher-tier testing.

In analogy, the environmental health program aimed at understanding and predicting emission routes, environmental fate processes, exposure of organisms, and (eco)toxicity of nanoparticles (Kolkman et al. 2013; Kettler et al. 2014; Meesters et al. 2014; Quik et al. 2014; Velzeboer et al. 2014;

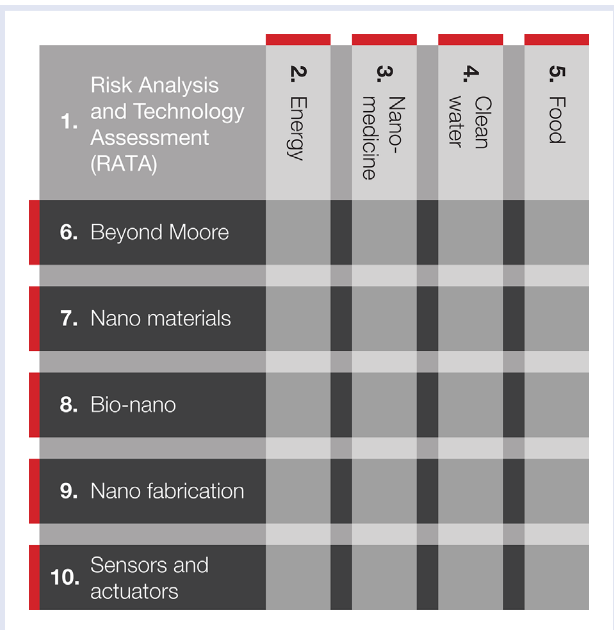

Figure 1. Themes in NanoNextNL.

Koelmans et al. 2015; Bäuerlein et al. 2017). Analytical methods to determine nanomaterials in environmental matrices were developed, as were models to predict environmental concentrations in various compartments. The obtained improved understanding of factors that govern environmental risks was applied to adapt tools for environmental risk analysis for nanomaterials.

The TA program (Bos et al. 2013; Te Kulve et al. 2013; Gupta et al. 2015; van Giesen et al. 2015; Alvial Palavicino 2016) studied the dynamics of nanotechnology developments and their embedding and impacts in society, including ethics, social equity and protection of norms, and public perception and engagement. This program also focused on governance questions for regulatory, ethical, and moral embedding of nanotechnologies.

DEVELOPED RATA PORTFOLIO AND EXPERIENCES

In addition to creating excellent science, the objective of NanoNextNL was to increase awareness of RATA by the scientists involved in the development and application of nanotechnologies that were active in the 9 other themes (Figure 1), and to develop and apply tools to guide a safe design and application of nanomaterials and nanotechnology. This was to encourage that safety and societal discussions keep pace with innovation processes, and to better safeguard that developments bringing unacceptable risks were identified and adapted at an early stage. Here, we describe the interaction with scientists involved in the development and application of nanotechnologies, as well as the procedures and products that were developed to enhance this interaction. In short our experiences included the following:

- Creating awareness of the supportive role of RATA in innovation processes
  - Two-day RATA course
  - RATA in PhD theses
  - RATA master classes and discussions
- Safe innovation tool
  - Development of a set of RATA awareness questions to valuate ideas in various technology readiness levels
  - Application in business cases
- Societal incubator as an added feature or analogous to a business incubator.

Creating awareness of the supportive role of RATA in innovation processes

Well-educated human capital is essential for responsible innovation (Sabadie 2014). To raise awareness among PhD students and other scientists involved for the role of RATA in early stages of innovation, a 2-day RATA course was developed. The course was followed by 83 persons within NanoNextNL, and focused on the basics of RATA and its potential role in early-stage innovation. The purpose,

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concepts, and paradigms of environmental and health risk analysis were introduced, and topics such as the innovation circle, public communication, and ethics were discussed. In addition, attention was paid to RATA questions related to the work of the participating PhD students, in preparation for a discussion on a specific RATA question in their PhD theses. Experienced RATA scientists supported defining topics to address in the respective PhD theses.

Many PhD students turned out to be highly interested in the topics discussed. Although RATA questions are often posed to them by family or friends, they are seldom discussed at the university department where the PhD students are employed. Their working environment is described by the students as a "protected space"; the interaction as opened by the course might help to create responsible innovation (Krabbenborg 2015). The course increased the RATA awareness among the NanoNextNL PhD students, other scientists involved, and their supervisors, and their understanding of the science within the RATA research program itself. Up to 1 to 3 years after the course, 78% of respondents to a questionnaire under RATA course participants answer that they know what RATA entails and how to implement it in their research (Margot Beukers, NanoNextNL, personal communication).

Fifty-six PhD students in specific programs within NanoNextNL were obliged to devote a section of their PhD thesis to RATA, out of a total of 225 PhD students involved. Risk analysis and technology assessment research was thus performed throughout the NanoNextNL program. In addition to the RATA course, PhD students were offered coaching by RATA scientists with expertise on their specific question; to date 10 students have made use of this possibility. Many PhD students chose to shortly reflect on RATA, and especially elaborate in their own specific scientific discipline. Some elaborated examples have however been published, such as work by Mulder (2016), who used TA to identify relevant applications and their characteristics for a sensor. Mulder concluded that a TA exercise is time intensive, and most beneficial close to the beginning of the project. Technology assessment makes the researcher aware of possible opportunities by anticipating future performance of the device. Another example is work in the water technology theme, where the treatment efficiency to remove fullerenes was studied as a way to minimize environmental and health risk (Floris et al. 2016). Some other examples are related to the sociotechnical aspects of plastics for culturing cells (Hulshof 2016) or the technological aspects and social embedding for a microfluidic bilayer (Stimberg 2014).

Finally RATA master classes were provided in Dutch nanotechnology conferences, directed to experienced scientists and supervisors. In program meetings of all nanotechnology application themes, RATA was discussed in relation to the topic of the specific program. Risk analysis and technology assessment theme events and specific workshops devoted to topics such as "safe-by-design" were open to interested scientists from other programs. Audiovisual material was developed (https://www.youtube.com/watch?v=T-mrx72qpVU). These activities helped to build an integrated network between technology developers and RATA experts, and to make supervisors more supportive in general to PhD students regarding their RATA work.

Safe innovation tool

To scale-up innovations from a low technology readiness level (TRL) to a higher TRL (EC 2014), many investments are required. Risk analysis and technology assessment can be integrated to guide "stage-gate" innovation (Cooper 2008), and in schedules and toolboxes to analyze business cases.

Based upon all discussions and interactions, we developed a set of easy-to-answer questions to check the RATA awareness behind an idea (Table 1). The questions in this "Safety and Society Check" can be posed at different TRL levels, and answers will be more elaborate and data rich farther along the innovation chain. We incorporated questions that point to a market opportunity (RA 1–2) and questions that make the product developer more aware about legislative frameworks in place (RA 3–5). Furthermore we stimulated the developers to reveal available data on hazard and fate (RA 6–8) and to think about possible emission pathways and mitigation strategies to limit emissions (RA 9–10). Then we included questions related to the stakeholders involved, their stakes, responsibilities, liabilities, and mutual relationship (TA 1–4). Finally, questions related to societal consequences are included (TA 5–6). When these questions in the Safety and Society Check (Table 1) are combined with common questions posed during business plan development (Figure 2), the answers yield a realistic insight into the possibilities of reaching the market phase and the investments needed, thereby increasing the chances of a successful business.

This Safety and Society Check, including the RATA awareness questions, was applied during scanning of business cases within NanoNextNL in order to challenge business development in start-ups and established companies. We learned that innovators generally have information that is also useful to screen for potential risks. This improved use of existing information reduces uncertainties.

Awareness of RATA aims to search for the lowest inherent toxicity and the highest functionality during the entire design phase, and also aims to be more compatible for application in a circular economy. If the use of inherently safe materials is not possible, manners of application of the material and of product use that prevent emission might be a second-best possibility. As a last and less favorable possibility, mitigation measures to prevent emissions and adverse effects can be included in the product design.

Societal incubator

Innovation processes can be hampered by "waiting games" (Parandian et al. 2012; Robinson et al. 2012; van Lente 2015) in which one actor waits for a second to make an important move. These waiting games more easily occur under high uncertainty, even if it is generally accepted that a technology is promising and further development is needed.

Table 1. Set of questions to check RATA awareness: What is the experience within your organization with risk analysis and technology assessment?

Risk analysis	Technology assessment
RA 1. Is your product less risky than existing products?	TA 1. Which other stakeholders, besides suppliers and customers, could you imagine?
RA 2. What are new aspects, related to already authorized products?	TA 2. How will these stakeholders be affected in both positive and negative ways?
RA 3. What is the "nano" aspect of your development?	TA 3. How does this new technology influence stakeholders' responsibilities and liabilities?
RA 4. What is the legislative framework for market introduction?	TA 4. How does this new technology influence the relationship between stakeholders?
RA 5. Are there any discussions on "nano" within this legislative framework?	TA 5. What is society missing out on, both positive and negative effects, if your idea does not reach the market?
RA 6. What do you already know on the safety aspects?	TA 6. Which different possible futures could you imagine with your development?
RA 7. Do you have any information on the intrinsic hazardous aspects?	
RA 8. Do you have information on the environmental fate and behavior?	
RA 9. Can material be released in significant quantities during the production, use, or waste phase?	
RA 10. Could you minimize emissions?	

RATA = risk analysis and technology assessment.

This waiting game created the idea of a "societal incubator" to allow experimentation and collective learning in areas of nanotechnology (van Lente 2015; Rerimassie et al. 2016), as an analog of and supportive to a business incubator in which a research findings are guided toward a commercial product. In the societal incubator, a range of precommercial applications is investigated for future possibilities and the variety of societal acceptance. Technology developers, businesses, and civil society stakeholders and organizations can explore possibilities for innovation, emphasizing urgent societal challenges. The societal incubator stimulates reflexivity about one's role in the novel technologies and their embedment in society (van Lente 2015). A societal incubator starts with a promising (nano)innovation for which there remain significant uncertainties concerning public support, policy, risk assessment, regulation, and liability. In the incubator information is collected and interaction organized, this is analyzed and then a decision is taken on further technology development (Rerimassie et al. 2016). During exploratory testing, it appeared that participants received the idea of the societal incubator as a positive contribution to prevent waiting games, and to shine light on their possible role in the innovation process. Actors such as regulators or consumer organizations are better able to adapt to the technological developments up front. A societal incubator might stimulate the success rate of new developments by offering an institutionalized protected space in which scientific and business developers, regulators, nongovernmental organizations (NGOs), and others have the opportunity to communicate openly and honestly, and to learn and share about specific new developments (for information on design and organization, see Rerimassie et al. 2016).

LESSONS LEARNED

Although there is much policy attention to responsible innovation and research funding is allocated to this theme, we are not aware of other examples of large programs on emerging technologies where RATA has really been integrated. Within NanoNextNL, the RATA theme was both articulated in a specifically devoted theme, as well as integrated in all themes of the whole program using the described portfolio.

The goal of RRI ultimately asks for full integration of RATA within research and development programs of emerging technologies (see also Walhout and Konrad 2015). Given that at present this full integration is still to be reached, we believe that the dual modus of dedicated RATA research and integration of RATA components across NanoNextNL (see Figure 1) that was chosen here is a good program structure. This dual modus ensures structural attention to and integration of RATA in technology development, and in subsequent business and policy making for new technologies, and seems unique in the international context (e.g., Fisher and Maricle 2015).

Awareness has grown for the benefits of linking technology assessment and risk analysis activities. Technology assessment helps to gain insight in potential pathways of

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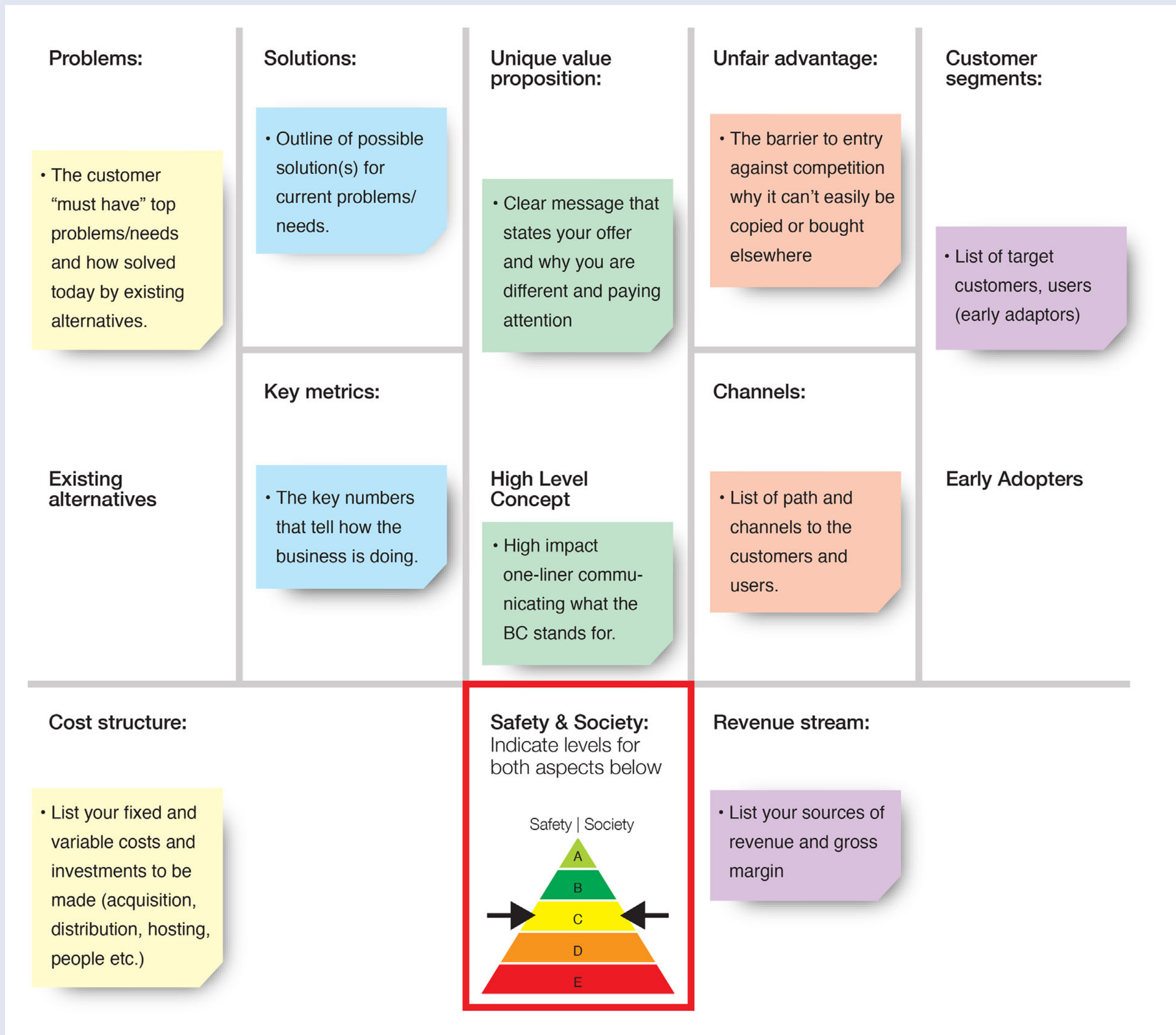

Figure 2. Safety and Society Check used to challenge, improve, and accelerate business development.

innovations and in identifying hurdles for innovators or regulators. In NanoNextNL, technology assessment was performed for cases in food, water, energy, and medicine, which helped to identify whether a lack of information on human and environmental safety was an obstacle for investors to support the creation of start-ups.

In NanoNextNL there were programmed stimuli for the interaction between RATA and the development and application of nanotechnologies. These could however be further strengthened by paying attention to this interaction from the start, for example, in consortia agreements and financial agreements signed per program in the starting period. Integration between RATA and technology development and application in the earliest phase possible, namely during the writing of research proposals, is a lesson to be further expanded and stimulated. Academic impetus, such as publications in highly cited journals, does not always stimulate the required multidisciplinary approach. However, technologically oriented scientists do see the strategic advantages of spending attention to responsible innovation in their own research, such as increased funding possibilities, increased speed of implementation, and societal acceptance of their work. Doctoral students also feel that they are better suited for a broader variety of job opportunities (Margot Beukers, NanoNextNL, personal communication).

A further possible improvement is the inclusion of design for circularity, in comparison to safe-by-design, in the approach, for example, concerning the recyclability of material or options to disassembly. Although use of scarce resources, such as space and energy, were at the start of NanoNextNL not considered as relevant as the safety and society questions explored, still these relevant aspects could be integrated in subsequent work.

CONCLUDING REMARKS

There is much policy attention to responsible innovation, and research funding has been allocated to this theme. However, there are not many large programs on emerging technologies where this is really been integrated (Khan et al. 2016).

NanoNextNL offers a unique network to explore how to put this into practice, where we focused on RA and TA as important contributors to responsible innovation. Activities such as courses and discussions in program meetings helped to build an integrated network between technology developers and RATA experts and to increase RATA awareness. Many scientists involved are highly interested in the RATA topics discussed. Within NanoNextNL the RATA theme was articulated separately in a specifically devoted theme, as well as integrated in the whole program using the developed portfolio. This dual modus is a good model to ensure attention to and integration of RATA in technology development, and subsequently in business and policy making. Linking TA and RA activities helps to gain insight, for example, into whether a lack of safety information is an obstacle for investors.

To scale-up innovations to a higher readiness level, RATA can be integrated to guide innovation and in business case analysis. As an integrated part of innovation, RATA intensifies interaction among innovators, RATA scientists, and regulators. A set of basic questions on RATA awareness is to be used, where answers will be more elaborate and data rich farther along the innovation chain. Innovators generally have information that is also useful to screen for potential risks.

The approach described also might inspire responsible innovation for other emerging technologies and is advised to be coupled up front to governmental investments in stimulating technology developments.

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Data Accessibility—Data associated with this research can be requested from the corresponding author by emailing annemarie.van.wezel@kwrwater.nl.

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