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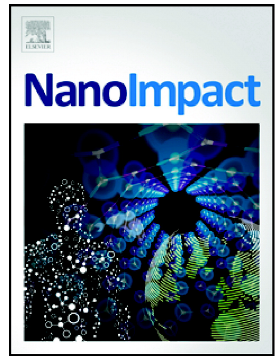

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Barriers to Responsible Innovation of Nanotechnology Applications in Food and Agriculture: A Study of US experts and Developers

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Abstract

The use of nanotechnology and engineered nanomaterials in food and agriculture (nano-agrifood) sectors is intended to provide several potential benefits to consumers and society, such as the provision of more nutritious processed foods, edible food coatings to extend shelf lives of fresh cut produce, and more sustainable alternatives to traditional agrochemicals. The responsible innovation of nano-agrifoods may be particularly important to pursue given previous case studies involving other agrifood technologies that experienced significant public consternation. Here, we define responsible innovation following Stilgoe et al. (2013) that establishes processes to iteratively review and reflect upon one's innovation, engage stakeholders in dialogue, and to be open and transparent throughout innovation stages – processes that go beyond primary focuses of understanding environmental, health, and safety impacts of nano-enabled products and implementing safe-by-design principles. Despite calls for responsible nano-innovation across diverse sectors, it has not yet been clear what types of barriers are faced by nano-agrifood researchers and innovators in particular. This study therefore identifies and builds the first typology of barriers to responsible innovation as perceived by researchers and product developers working in nano-agrifood sectors in the United States. Our findings report 5 key barriers to responsible innovation of nano-agrifoods: *Lack of Data* (reported by 70% of all interview participants, and represented 34.6% of all barrier-related excerpts), *Lack of Product Oversight* (reported by 60% of participants, and represented 28.7% of excerpts), *Need for Ensuring Marketability & Use* (reported by 70% of participants, and represented 21.3% of all barrier-related excerpts), *Need for Increased Collaboration* (reported by 40% of participants, and represented 10.3% of excerpts), and finally *Lack of Adequate Training & Workforce* (reported by 30% of participants, and represented by 5.1% of excerpts). We also relate these key barriers across three main nano-innovation phases, including 1) Scientific and Technical R&D, 2) Product Oversight, and 3) Post-commercialization Marketability & Use, and discuss how these barriers may impact stakeholders as well as present opportunities to align with principles of responsible innovation. Overall, these findings may help illuminate challenges that researchers and innovators face in the pursuit of responsible

innovation relevant for the field of nanotechnology with relevancy for other emerging food and agricultural technologies more broadly.

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1. INTRODUCTION

The responsible development and innovation of nanotechnologies has been a priority within national and international strategies of nano-research and development (R&D) for more than 15 years (NNI, 2020; EU 2008). It has been important to include mechanisms for responsible nano-innovation to not only better account for the potential impacts of nanotechnology "upstream" of technology development (i.e. in early stages of innovation before R&D directions are established), but also to include stakeholders and diverse publics in dialogues about nano-enabled products and to be responsive to public and stakeholder concerns. For example, the National Nanotechnology Initiative (NNI) in the United States (U.S.) has devoted one of its four strategic goals towards the responsible development of nanotechnology and nano-enabled products among other goals of developing a world-class R&D program, fostering technology transfer, and developing education and workforce (NNI, 2020). In addition to various and wide-reaching applications, nanotechnology and engineered nanomaterials are currently being developed and used in a range of food and agriculture applications, including e.g. food additives, food supplements, agrochemical formulations, and veterinary medicines (Setyawati et al., 2020, Nile et al. 2020, Sampathkumar et al., 2020). Their use in food and agriculture sectors are intended to provide several potential benefits to consumers and society and may contribute to more sustainable food and agricultural practices through e.g. enhanced nutrition, improved food properties, and more efficient delivery of agrochemicals. At the same time, the full impacts of diverse nano-agrifood applications on health, the environment, as well as society is not fully understood, and research continues to investigate environmental, health, and safety (EHS) as well as ethical, legal, and societal impacts (ELSI) of nano-agrifood products and sectors (e.g. Baranowska-Wójcik et al., 2020; McClements and Rao, 2011).

The responsible innovation of nanotechnologies used in food and agriculture may be particularly important to pursue given previous experiences with other emerging agrifood technologies that experienced significant public consternation (e.g. first generation of GMOs). In this paper, we define responsible innovation following Stilgoe et al. (2013), as "taking care of the future through collective stewardship of science and innovation in the present" (page number 1570). Stilgoe et al. (2013)'s definition also relies on four main pillars of anticipation (i.e. to anticipate potential impacts and effects), inclusion (i.e. to include diverse perspectives and views), reflection (i.e. to reflect upon one's motivations and assumptions), and responsiveness (i.e. to respond and adapt to new information, stakeholder values, concerns, etc.). We note that other definitions of responsible innovation have also been proposed, including those that highlight transparency, openness, sustainability, and care (Fraaje et al., 2019; Owen et al. 2019; Burget et al. 2017). Overall, these definitions and views of responsible innovation are much broader and more inclusive than primarily considering EHS impacts of nanomaterials of nano-enabled products, developing and implementing safe-by-design principles, green chemistry, and/or including ELSI considerations. Rather principles of responsible innovation establish processes and mechanisms to continually and iteratively review and reflect upon one's innovation, include and incorporate mechanisms for stakeholder engagement and dialogue, and to be open and transparent throughout innovation stages. In the case of responsible innovation of nanotechnologies in food and agriculture sectors, it seems particularly important to ensure responsible innovation practices occur given recent studies that have demonstrated heightened relative levels of concern for nanomaterials used in food and agriculture compared to other applications (e.g. electronics, energy, automotives) (Porcari et al. 2019; ECHA 2020), consistent with previous studies on nano-risk perceptions in food and other consumer products (Chuah et al. 2018; Cummings et al. 2018; Siegrist and Keller 2011; Steenis and Fisher 2016; Yue et al. 2015a, 2015b).

While significant progress has been made to understand potential impacts and concerns of nanomaterials and nano-enabled products within the past 15+ years (Grieger et al. 2019; Friedersdorf et al. 2019), including the conduction of studies on nano-safety and perceptions of nano-agrifoods according to different stakeholders (Stone et al. 2020; Johnston et al. 2020; FDA 2020; ECHA 2020; Pillai & Bezbaruah 2017; Feindt & Poortvliet 2019; Zhou & Hu 2018), it has not yet been clear if and how nano-agrifood innovations have incorporated these research findings back into (responsible) product design, development, and commercialization, including if and how nano-agrifood innovators have incorporated safe-by-design principles. While others have reviewed if and how responsible nano-innovation has occurred more broadly (e.g. Shelley-Egan et al. 2018; Maynard 2015; Lin 2016), it has not yet been clear if and how responsible innovation practices have occurred specifically for nano-agrifoods.

In addition, while there has been a consensus on the need for responsible nano-development and innovation, some have reported potential barriers to its practices, including challenges to embedding responsible innovation within nano-research and innovation organizations and the lack of institutionalization of responsible innovation practices (Shelley-Egan et al. 2018) as well as barriers to launching new businesses and developing new nano-enabled products (Maynard 2015). Further, others have identified barriers to responsible innovation in biotech-innovation systems and developed frameworks for categorizing them by micro-levels of the individual, such as attitudes that actors and stakeholders hold; meso-levels of institutions, such as organization structures like funding or other incentives; or macro-levels of broader contexts, such as political, economic, cultural, and social systems (Kuzma & Roberts 2018; Roberts et al. 2020). Others still have noted that barriers are contextually-based, and innovation processes need to be customized as 'one size fits all' approaches are likely to be ineffective (van de Poel et al., 2020).

Given that food and agriculture may be among the most important sectors to ensure and demonstrate responsible innovation of nanotechnology, it is important to highlight and describe potential barriers that may exist for responsible innovation within nano-agrifood sectors. A better comprehension and capturing of potential barriers to responsible nano-agrifood innovation is critical not only to help ensure the sustainability of these products and applications, but also to reflect on best practices relevant for other emerging food and agricultural technologies. Our analysis therefore aims to fill this important gap by highlighting key barriers that nano-agrifood researchers working in industry and academia face to responsibly innovate, based on 20 semi-structured interviews[1].

To guide our inquiry, we forward the research question, “According to researchers and innovators of nano-agrifoods, what are the most prominent barriers to responsible development and innovation?” This analysis therefore presents key findings of barriers to responsible innovation of nano-agrifoods as distilled from research interviews from nano-agrifood sectors and discusses how these findings relate to the broader context of responsible innovation of new technologies in food and agriculture.

2. METHODS

We conducted 20 semi-structured interviews with researchers from industry and academic institutions in the U.S. involved in nano-agrifood R&D and commercialization. The data collection, respondent communication, and analysis all conformed to the IRB statutes approved by the grant PI’s university (PI = Grieger; NC State University, IRB protocol 19207). We sought a heterogeneous sample of expert participants that would report the breadth and depth of perceived barriers to responsible innovation of nanotechnology-enabled food and agriculture research and development. Study participants were identified through author index searches of peer-reviewed manuscripts and reports on nanotechnology use in food and agriculture sectors, including food processing, food production, agrochemical development and use, and veterinary medicine. We further identified potential study participants by reviewing the USDA Current Research Information Systems (CRIS) database as well as publicly-accessible websites developed by nano-agrifood companies and research institutions. Our searches were limited to materials written in the English language. Our search yielded 95 prominent U.S. based experts in the field, 50 of whom were affiliated with academic institutions while the remaining 45 of worked in food and/or agricultural industries. All identified experts were invited to serve as study participants via email from the research team. Twenty individuals, including 8 from industry and 12 from academic institutions, agreed to serve as interview participants. Study participants were involved in a range of nano-agrifood sectors, including nanomaterials used in pesticide and fertilizer formulations, food processing, dietary supplements, and in veterinary medicine. Most participants hold a Master’s or terminal degree (e.g. PhD) in their respective field and all have either published peer-reviewed research papers or reports, or are featured in the CRIS database, and/or working as researchers or innovators in nano-agrifood sectors.

Following our IRB-approved protocol to conduct the study, all study participants completed a signed informed consent process prior to conducting the interviews. The interviews were held via an online meeting platform between December 2019 and June 2020 and lasted 60-75 minutes in duration. All interviews were audio-recorded and transcribed, and the interviewer

[1] This work is a part of the USDA/NIFA-funded grant *Social Implications and Best Practices for Responsible Innovation of Nanotechnology in Food and Agriculture*; Grant No. 2019-67023-29855).

took extensive notes during the interviews for use during subsequent analysis. All interviews were confidential and only de-identified data were used in analysis and reporting. The interviews followed a semi-structured interview protocol, and planned questions were sent in advance to study participants. The interviews focused on a range of topics including definitions, motives, and practices for enacting responsible innovation, which are reported in other publications under development (Kokotovich et al. 2021 – *in review*). This analysis highlights findings primarily from the following question: "From the perspective of your company/organization, what are the challenges you face as you try to innovate responsibly with nanotechnology?" As our study was centered on the barriers as identified by researchers and developers, it does not include barriers that may be identified by other stakeholders. As will be detailed in our results section, barriers perceived by study participants may not be perceived of as barriers by other stakeholder groups. For instance, our study participants commonly voiced that a lack of regulatory guidance is a significant barrier to responsible innovation of nano-agrifoods, although it seems reasonable that individuals working in government policy arenas may perceive this issue differently and/or may not perceive it to be a barrier at all.

Data management and approach to analysis

To develop a typology of barriers for responsible innovation of nano-agrifoods, we followed the data management and qualitative analytical approach of Halcomb and Davidson (2006), and which has subsequently been adapted for use in related theory-building work regarding emerging science trust issues (Cummings et al. 2021 - *in review*). As noted earlier, barriers were a prioritized topic of interest among informants, but it was only one subset of a variety of topics focused on responsible innovation discussed in the interviews. As such, following the completion of each interview, a research team member documented the significant issues reported by the informant. This reflective process allowed the research team to develop summarizing field notes that would prioritize more granular inquiries following the completion of all interviews. Full transcripts of audio files were created and uploaded to Dedoose, a secure web application for mixed-method research. We used this platform primarily for organizational purposes and to house the full compendium of textual interview data. During the transcription process and field-note reflections, the research team returned to the raw audio files as warranted to identify and ensure accuracy of verbatim illustrative quotes that would be used to exemplify key responsible innovation barriers within the typology. This approach can help minimize interviewer biases and provide more robust cross-case comparisons of research findings. The specific information on nano-agrifood responsible innovation from the 20 interviews was subsequently collated into a 28,000-word compendium of direct text from respondents which was used for this study's analysis.

Using this compendium, the lead author then approached the data from a grounded theory perspective. This approach prioritizes theoretical sampling where the objective is to "explore the dimensional range or varied conditions along which the properties of concepts vary" (Strauss and Corbin 1998, p. 73). To achieve this result, the research team employed the constant comparative method where each textual excerpt related to responsible innovation barriers was compared against one another. This inductive form of assessment allows for the emergence of the typology's themes without inducing *a priori* assumptions of the content or form of the responsible innovation barrier under investigation. In doing so, this process allows for robust and granular themes to surface from patterns in the data without presupposition of what themes may or may not be present among participant responses (Patton 2002). This constructivist approach is a cornerstone of theory-building where description and explanation of interview contents can be identified and organized to systematically inform how this expert group envisions barriers to responsible innovation of nano-agrifoods. The themes reported within this typology are also developed primarily through *in vivo* coding which seeks to reflect the "vernacularity" of the informants' responses (Given 2008). Thus, the labels describing themes within the typology correspond first to concepts and diction used by the informants themselves which better typifies the barriers this group recognizes that may impeded nano-agrifood research and development.

3. RESULTS

We report our findings on key barriers to responsible innovation of nano-agrifoods in the resulting typology. In total, we identified 5 key barriers to responsible innovation of nano-agrifoods: *Lack of Data* (reported by 70% of all interview participants, and represented 34.6% of all barrier-related excerpts), *Need for Ensuring Marketability & Use* (reported by 70% of participants, and represented 21.3% of all barrier-related excerpts), *Lack of Product Oversight* (reported by 60% of participants, and represented 28.7% of excerpts), *Need for Increased Collaboration* (reported by 40% of participants, and represented 10.3% of excerpts), and finally *Lack of Adequate Training & Workforce* (reported by 30% of participants, and represented by 5.1% of excerpts) (Table 1). Each of these key barriers along with sub-barriers are explained in further detail below.

In addition, these barriers are conceptualized according to three main innovation phases using traditional innovation paradigms (e.g. Cooper 1990, Shandilya et al. 2020). These innovation phases include 1) Scientific and Technical R&D, which traditionally includes initial ideas and brainstorming, development of prototypes, product development, testing, and production finalization; 2) Product Oversight, which traditionally includes regulations, guidelines, guidance, and other mechanisms to monitor and ensure product safety and compliance, such as e.g. voluntary information provisions; and 3) Post-commercialization and Marketability & Use, that traditionally includes aspects of monitoring consumer and stakeholder acceptance, public perceptions, and other aspects to ensure product success and sustainability (Table 1). This approach to conceptualizing key barriers elucidated by study participants was designed to help identify important innovation phases where barriers to nano-innovation may occur and which stakeholders may be impacted, as further elaborated on in the Discussion. We should note here that the innovation phases included in Table 1 represent three key areas of innovation as described by the interviewees in their description of barriers to responsible nano-innovation, also aligning with current literature on nano-innovation (e.g. Franken et al. 2020, Shandilya et al. 2020), and do not aim to represent an ideal innovation pipeline that whole-heartedly follow principles of responsible innovation with more open, iterative, anticipatory, and inclusive innovation processes and cycles (Stilgoe et al. 2013).

Table 1. Frequency and Distribution of Barriers to Responsible Innovation of Nano-Agrifoods across Innovation Phases. Results are displayed both as frequency (number) and percentage of excerpts across all interviews as well as frequency (number) and percentage of interviewees who reported the barrier(s). Total results related to primary barriers are shown in bold.

Innovation Phase	**Barriers to Responsible Innovation**		**Excerpts That Mentioned Barrier**		**Interviewees Who Mentioned Barrier**	
	Primary	**Sub-Barriers**	**Frequency**	**% of total**	**Frequency**	**% of total**
Scientific & Technical R&D	1. **Lack of Data**		**47**	**34.6%**	**14**	**70%**
		Lack of Consistent Product Control	5	3.6%	4	20%
		Insufficient Long-term Risk Evaluations	15	11%	7	35%
		Uncertainty of Nano-safety in Field Studies	18	13.2%	10	50%
		Low Reproducibility of Studies	9	6.6%	5	25%
	2. **Lack of Adequate Training & Workforce**		**7**	**5.1%**	**6**	**30%**
	3. **Need for Increased Collaboration**		**14**	**10.3%**	**8**	**40%**
Product Oversight	4. **Lack of Product Oversight**		**39**	**28.7%**	**12**	**60%**
		Lack of Regulatory Guidance	29	21.3%	11	55%
		Lack of Regulatory Gatekeeping	10	7.4%	7	35%
Post-Commercialization Marketability & Use	5. **Need for Ensuring Marketability & Use**		**29**	**21.3%**	**14**	**70%**
		Lack of Trust	19	14%	11	55%
		Skepticism of Product Efficacy	10	7.4%	7	35%
			Total = 136	**Total = 100%**		

3.1 Scientific & Technical R&D Innovation Phase

All 20 interview participants reported on the barriers to responsible innovation of nano-agrifoods related to the scientific and technical challenges of product R&D phases. These scientific and technical R&D barriers included those related to a *Lack of Data*, related to not only foundational aspects of developing new or novel nano-agrifood products (such as a lack of consistent product control and low reproducibility of studies), but also to lack of data related to understanding their potential EHS implications, including insufficient long-term risk evaluations and uncertainty of nano-safety in field studies (Table 1). In addition, interview participants reported on having a *Lack of Adequate Training and/or Workforce*, as well as the *Need for Increased Collaboration* among research teams. Each of these main barriers and sub-barriers are further described below.

3.1.1 Barrier 1. Lack of Data

The interview participants noted that to responsibly innovate, one must have robust and granular knowledge and reliable data regarding the science, process, and safety-evaluations of all components and applications of a product under development. As a corollary to this foundational premise, the most widely reported barrier to the responsible innovation of nano-agrifoods that was reported by study participants was the concern that there is currently a significant *Lack of Data*, mentioned by 70% of interviewees and accounted for 34.6% of all barrier-related excerpts from interviews. The lack of data manifests in multiple ways including (in order to decreasing prominence): *Uncertainty regarding nano-safety in applied field use* (mentioned by 50% of interviewees, and representing 13.2% of excerpts); *Insufficient long-term risk evaluations* (mentioned by 35% of interviewees, and representing 11% of excerpts); *Low reproducibility of research studies* that evaluate product development and product-related risks (mentioned by 25% of participants, and representing 6.6% of excerpts); and *Lack of consistent product control* (mentioned by 20% of interviewees, and representing 3.6% of all excerpts) (Table 1). We find value in elaborated discussion of each of these sub-themes, as this was the most discussed barrier within our typology.

3.1.1.1*Lack of Consistent Product Control*

Foundational to the development and use on novel nano-agrifood products is the reliable production of nanomaterials and nano-agrifood products that demonstrate consistent performance. Many experts noted the technical difficulty in nanomaterial production that ensures the product holds its size and shape to a suitable standard and is composed properly to deliver stable and consistent performance as intended by its design. As one expert said, “it’s very hard to make the nanotechnology or nanomaterial consistently [and] to control precisely its properties… just getting up the production, the synthesis, requires a lot of effort” (Interviewee A03). Across all sub-barriers in the overarching *Lack of Data* theme, this sub-barrier was cited least frequently with 20% of interviewees mentioning this barrier and represented by 3.6% of all interview excerpts.

3.1.1.2 Insufficient Long-term Risk Evaluations

Many respondents also noted that a key barrier to responsible innovation is the lack of established safety data as would be demonstrated by longitudinal toxicological studies of nano-agrifood impacts on humans, animals, and the various environments in which they may be used. In total, 35% of all interviewees mentioned *Insufficient long-term risk evaluations* as a barrier to responsible innovation, and there were 15 excerpts (representing 11% of all excerpts) relating to this sub-barrier. As one expert stated: "we need long-term study" (Interviewee A02). This sentiment was echoed by many other respondents who provided more nuances to the current insufficiencies in longitudinal risk assessment of nano-agrifood applications. For instance, one expert identified the likelihood that current methods for evaluating negative impacts of nanoparticles involve "high concentrations" which may lead to "overestimating its toxicity" and that there are "very few studies on long-term, low-dose nanomaterial toxicity" and that while "a lot of people are advocating them, you still see very few studies" (Interviewee A03).

Further, resource allocation including time and funding was noted by some interviewees as a primary driver for the insufficiency found in long-term risk evaluation. For example, one interviewee stated: "One of the big challenges is the time that it takes to run a [toxicological] study. You grow a plant, and you can grow it for three weeks and make a bunch of measurements or you can grow it for 90 days, all the way to fruit and make measurements. Those studies just take a really long time. They are expensive. There is never money in budgets to do things for that long" (Interviewee A09).

3.1.1.3 Uncertainty Regarding Nano-safety in Applied Field Use

Many study participants voiced similar concerns regarding the difficulty in evaluating nano-agrifood product safety in the field. For example, half of all interviewees (50%) mentioned this sub-barrier of *Uncertainty Regarding Nano-safety in Applied Field Use* in interviews, and there were a total of 18 excerpts (13.2% of all excerpts) (Table 1). As one expert said, "developing responsible materials is fine, but then, proving that they are safe is the challenge. How do you track these particles? They are carbon, hydrogen, oxygen, how do you track them in a plant? Common methods used for metallic particles tracing do not apply here" (Interviewee A08).

One reason for the high uncertainty regarding the safety of applied field use of nano-agrifood products is due to the lack of scientific instruments (tools and other instrumentation) as well as robust evaluation protocols (guidelines and testing strategies) that could establish empirical data suitable for *in situ* risk assessment. This is a data challenge tied to the lack of regulatory guidance, discussed below, and may hinder early product development as innovators note they are unable to demonstrate safety of their products should they be forwarded for use in various agricultural settings. As one expert noted, "EPA and FDA are very keen on this, they want more information to accurately define and establish the safety protocols for nano-based approaches. However, right now, they're unable to do this because of the lack of tools—for example, the tools to look at the fate, whether these particles stay in the environment by itself (Interviewee A12)."

3.1.1.4 Low Reproducibility of Research Studies

Some participants noted that the lack of methodological standards or best practices in conducting research in this nascent field has rendered much of the research literature to be “disjointed” (Interviewee A07); leading to *Low reproducibility of studies* where researchers have difficulty in identifying or replicating how others are conducting their work. This sub-barrier was mentioned by 25% of all interviewees and included in 9 excerpts (corresponding to 6.6% of all excerpts) (Table 1). This sub-barrier is illustrated by one interviewee: “not having standardized methods means that… we are each using our own slightly nuanced approach” which has fostered “results that are not directly comparable” (Interviewee A07).

3.1.2 Barrier 2. Lack of Adequate Training & Workforce

Another reported barrier to responsible innovation within the scientific and technical R&D stage is the lack of adequately trained, educated, and interested workforce that is needed to produce and evaluate nano-agrifood products. This barrier was mentioned by 30% of interviewees and represented 5.1% of all barrier-related excerpts identified in this study (Table 1). This was typified by one of the academic researchers who said, “honestly, one challenge is finding good PhD students that really are interested in this problem, not all of them want to do agriculture research, they want to do remediation and they want to look at heavy metals and organics and environments, not necessarily food” (Interviewee A09). Another respondent echoed this in saying, that a primary barrier to responsible innovation is “not having enough people or talent to be able to recruit into this field to do more work. Not having enough places of employment for my graduate students to fall into after they finish training in my laboratory” (Interviewee A11). These researchers highlight the difficulty of finding students who have both an interest in nanotechnology and interest and expertise in agricultural systems.

The complexity of this applied field which demands interdisciplinary knowledge structures and teams to carry out leading-edge research may be the root cause that dissuades young professionals from entering this field. As noted earlier in this paper, nano-agrifood applications are plagued by physical environmental systems-level complexity where innovations must incorporate diverse experts and stakeholders vested in seeking adequate answers to often “wicked” problems. As one expert said, “it's so interdisciplinary and because there's so many stakeholders and because the environment is so complex, it's like everybody has their focus and so scoping a project is really challenging… you can’t get to a field study scale before you have the technology developed at the lab scale… the complexity of the system makes it really interesting but it also makes it really challenging” (Interviewee A07).

3.1.3 Barrier 3. Need for Increased Collaboration

Another main barrier to responsible nano-agrifood innovation that arose from the interviews were challenges related to collaboration with outside partners. Forty percentage of interviewees mentioned this barrier, also represented by approximately 10.3% of all barrier-related excerpts identified in the study (Table 1). The types of collaborations called for varied across participants, from those to ensure products could reach the market to those to ensure that products could be safely tested. For example, one participant noted that “we don’t really have an industrial partner” and that one would be needed to further advance this innovation towards deployment as a product (Interviewee A02). Further and related to the barrier of collaborating more generally was the barrier to obtain information and data from collaborators to pursue nano-agrifood R&D and innovations. One participant noted the potential limitations of collaborating with another entity when, for example, “they won't give out data because they control that part of the market” (Interviewee B02). Another interview participant noted a barrier to not sharing data that may raise ethical issues: “if you have that sort of information and keep it to yourself, there's also an ethical issue there if you're finding something bad. So I think this is really the argument for why this kind of research needs to be in the public sector and providing everyone with a level playing ground for being able to make decisions and also for regulators to clearly base regulations on information that everyone can evaluate” (Interviewee A06).

Related to the need for collaboration to ensure safety of products, other interview participants expressed difficulties in finding collaborating partners to help conduct studies for both investigating field study sites as well as for conducting safety studies. For example, one interviewee stated “You need to have strong partners. You don’t want to contaminate the environment. You don’t want to contaminate the processing. So, you have to find strong partners who is willing to allow you to do the testing in their facility or in the field.” (Interviewee A04).

3.2 Product Oversight Innovation Phase

3.2.1 Barrier 4. Lack of Product Oversight

From our interviews with nano-agrifood researchers we identified a key barrier to responsible innovation related to a lack of sufficient product oversight. Sixty percent of interviewees mentioned the *Lack of Product Oversight* as a challenge to responsible innovation, also representing 28.7% of all barrier-related excerpts (Table 1). These relate to similar oversight and regulatory challenges for nano-agrifood applications identified previously which are complicated by the complexity of nanomaterials, diversity of food and agriculture products in which they may be used, and difficulties of regulatory frameworks and mechanisms to easily and quickly adapt to nano-specific properties and behavior (e.g. Grieger et al., 2016a, 2016b; Aschberger et al. 2014, Sandoval 2009, Suppan 2011, Xiaojia et al. 2018). Further, the lack of data (as noted earlier) coupled with complexities of nano-agrifood products have hampered oversight and regulatory mechanisms for nano-agrifoods. This overarching barrier related to the *Lack of Product Oversight* was then further characterized by two additional sub-barriers: *Lack of Regulatory Guidance* (mentioned by 55% of all interviewees and comprised of 21.3% of all excerpts) and *Lack of Regulatory Gatekeeping* (mentioned by 35% of interviewees and comprised of 7.4% of all excerpts).

3.2.2 Lack of Regulatory Guidance

Some experts noted that responsible innovation can be hindered by the (perceived) inability of government agencies to provide guidance about regulatory structures, policies, and processes related to product safety and approvals for commercial use. This was discussed by our participants often as a lack of clear regulation which challenges innovators to be clear and certain of regulatory needs during product development. As another expert informally stated, "Nano is a crazy hot mess of things in terms of the U.S. Government … the U.S. Government won't quite say what is okay and what is not okay" (Interviewee B05). This barrier may also touch upon the cumbersome collaborations between distinct agencies with overlapping authority in this interdisciplinary area where, for example, some nano-agrifood applications could be perceived to fall under the purview of different agencies including the FDA, USDA, EPA, and/or and other agencies (such as Consumer Product Safety Commission) who may each demand (or disregard) particular, and different, data related to safety, transport, fate and disposal of nanomaterials. This regulatory landscape is viewed of as difficult to traverse as our expert noted, "some of the regulatory frameworks can slow things down." (Interviewee B07).

The potential lack of clear and proscriptive communication regarding the oversight process may leave innovators in this area to experience uncertainty in terms of if or how to proceed with nano-agrifood innovations overall, if and how to provide nano-specific safety data, whether they should seek independent third-party counsel, and/or compile a patchwork approach to demonstrating product safety. For example, one researcher noted, "If you know the requirements that EPA and FDA might throw at us, we can start working towards, you know, answering those things right away, but if those things show up at the last minute, you know, we are on the 11th hour of registration and then they come up with well you need to do all of these, then that puts us back into the start line. So, that's a concern. But then we know that the agencies are simply not there with the regulations in this aspect" (Interviewee B04).

This lack of clear guidance and view of regulation as overly burdensome can even lead some investors to avoid nanotechnology all together, as one interviewee said: "I have also seen it be very stifling for innovation because of it would take millions of dollars and multiple years to get through the regulatory hurdles, and venture capitalists don't want to invest with that kind of a dollar value time horizon so they just walk away from it" (Interviewee B07). This lack of guidance also impacts other instances of oversight, as other researchers also noted a reticence to approve nano-agrifood research by the Institutional Review Boards at universities. One of our academic researchers went as far to say, "[T]he IRB at a lot of the universities most likely would not approve a nanoparticle-fortified food for consumption. They're not sure about safety" [Interviewee A02].

3.2.3 Lack of Regulatory Gatekeeping

The other product oversight barrier of responsible innovation of nano-agrifood products is the (perceived) lack of gatekeeping by regulatory authorities. In this sense, gatekeeping refers to the responsible arbitration of product safety demonstration by regulatory authorities prior to product approval. This can include demands and solicitations of producers made by authorities for product-risk information as well as adequate scrutiny prior to product approval. For many applications of nano-agrifood technologies the “gate” seems to be wide-open with few restrictions or processes that would ensure products are safe and effective. As one expert said, “It’s a “Wild West” in [nano]fertilizers, if you’re the manufacturer of an engineered nanoparticle, you just need to make a disclosure of what you’re manufacturing and where it goes, and if that nanomaterial is not made of a toxic substance, then you’re more or less good to go... give the EPA a call, and they’ll say, “yeah we don’t regulate fertilizer”… so all fertilizers are registered through individual states and all states with the exception of maybe two that we’ve interacted with don’t even give a second thought about the environment. That [nano-fertilizers are] regulated, if at all, [they are] regulated on a watershed level or on a water system level” (Interviewee B08). This ad hoc disclosure system may be viewed as enabling products that would not pass more stringent regulatory processes to enter the market, thereby lowering the feasibility that they have been innovated responsibly and may pose greater, yet unassessed, risks.

3.3 Post-Commercialization Marketability & Use Innovation Phase

3.3.1 Barrier 5. Need for Ensuring Marketability & Use

Following successful development, safety testing, and regulatory approval of a product, innovators then aim to promote their product for industrial use by consumers, industry, and other stakeholder groups. However, many of our experts noted that even if they responsibly develop a product and gain regulatory approvals, it may still not be accepted or used by their consumers and other stakeholders. In fact, barriers to ensuring marketability and use were mentioned by 70% of interviewees and accounted for 21.3% of all barrier-related excerpts in our study. Experts stressed that some of the biggest barriers to responsible innovation of nano-agrifood products stem, in fact, from fears that even if they develop an idyllic product that provides wide benefits, is safe, and cost-effective, they may still be rejected by consumers who distrust nanotechnology or are skeptical of the product’s efficacy to provide the benefit and risk profiles identified by developers. This overarching barrier related to *Ensuring Marketability & Use* was further characterized by two sub-barriers: *Lack of Trust,* mentioned by 55% of interviewees and comprised of 14% of all barrier-related excerpts, and *Skepticism of Product Efficacy*, mentioned by 35% of interviewees and 7% of all excerpts (Table 1).

3.3.2 Lack of Trust

Some of interview respondents noted that a significant barrier to innovation is tied to the lack of trust in nanotechnology, and perhaps emerging technologies more generally. As one expert said, “The great challenge with nanotechnology is exactly the same challenge that we have with genetic modification technology, the matter that the public doesn’t really understand them, and we are really struggling not to prove their value or worth economically or sustainably, but simply whether or not the public trusts the technology” (Interviewee B03). The dynamics of trust in emerging products are related to the product itself but also to consumer judgments of the trustworthiness of key organizational actors including developers and regulators—should consumers hold concerns about the motives of these groups, they are more likely to reject a product.

The lack of trust was also brought up by some experts as related to the products being "nano," which may serve a heuristic cautionary function for some consumers that may dismiss the product based on subject-matter ignorance. For instance, one expert said, "the risk is there like any other chemicals but look at the benefits. Benefits for the environment, benefits for the growers, benefits for the industry people who will be selling this product and really the benefit is more than the risk, then why not nanotechnology? It is literally just another empowering technology. So, not to be scared that "oh my god, this is a nano" (Interviewee A10).

3.3.3 Skepticism of Product Efficacy

While certainly related to a lack of trust, skepticism is manifest in stakeholders' questioning of claims about nano-agrifood products that are made by product proponents. Skepticism is distinct from trust, as trust is ascribed to an actor or their product while skepticism relates more to the doubts and justifiability of claims related to those actors or products. Skeptics maintain beliefs that there is insufficient knowledge or data to settle any doubts about product claims. For instance, one expert said, "will your customers accept your new product, or will they say "oh, we don't want to use that because we're not really sure if it will do what you said it would do" (Interviewee B06). Skepticism may persist even in the presence of efficacious and safe product development as data and claims may continually be refuted or rejected by could-be consumers as they believe the knowledge or beliefs of product proponents are bogus or themselves suspect. When speaking of new nano-agrifood applications one expert went as far as to say that many involved in agriculture "just think it's snake oil." When asked to elaborate, the expert said, "[For instance] they don't think there's a product out there that can change pH. I can change pH of soil. You give me three months and I'll change your pH organic matter in the soil. I've got proven results of doing this. But even your PhDs out there don't understand it and they think it's snake oil" (Interviewee B02).

3.4 Business-related Barriers to Nano-agrifood Innovation

While our typology reports barriers specific to responsible nano-agrifood development and innovation (as shown in previous sections), our interviews with nano-agrifood researchers and innovators also commonly voiced three other barriers endemic to R&D specific to start-up companies or venture businesses (termed hereafter as "business barriers"). Note that we have not included these data related to business barriers alongside the Primary and Secondary barriers listed in Table 1, since they are primarily related to challenges to nano-agrifood businesses more broadly rather than having a focus on responsible innovation. However, since they were pronounced by the interviewees, we felt it was nonetheless important to include here.

Lack of Access to Adequate Funding for R&D. The most common business barrier identified was a *Lack of Access to Adequate Funding for R&D*, mentioned by 40% of interviewees and comprised 27.3% of business barrier-related excerpts. Participants noted that funding is a general and foundational barrier as financial backing is needed throughout innovation stages to e.g. pay salaries of workers and collaborators, provide materials and physical infrastructure, conduct risk assessments, and market products to potential consumers. As one participant said, “Funding. That’s the bottom line. It is always longer and more expensive to commercialize a product than you first think, and you make a proposal and you can get funding from somebody who thinks it should take you half the time and half the budget” (Interviewee B07).

Competition with Better Resourced Companies. The second notable business barrier that arose from our interviews and which is also related to a lack of funding, was the inherent *Competition with Better Resourced Companies*, mentioned by 10% of interviewees and comprised 6.1% of business barrier-related excerpts. As noted previously, interviewees from industry mostly represented small-to-medium sized companies who shared similar views with this researcher who said, “the cost of doing R&D is becoming prohibitively expensive, but at the same time it is a necessity… we are a smaller company, so we are going against these bigger companies who have a lot more people on the ground to sell their products that would throw millions and millions of dollars to sales and marketing. We would be at the losing edge if we really go against them” (Interviewee B06).

Pressure from Market-based Motives. The third business barrier was *Pressure from Market-based Motives* to ensure profit margin increases, mentioned by 35% of interviewees and comprised 36.4% of business barrier-related excerpts. In this case, participants noted challenges stemming from profit-driven commerce models as well as the fact that many projects are stymied by limited expected margins even if the anticipated product would prove safer and more sustainable than rival products. Some participants noted that the drive to increase profits for shareholders may even result in comprised self-identity as a responsible innovator, where one participant noted, “the biggest challenge is the pressure to make money for the company, and the pressure to let your values, or let the things that you claim to hold dear, [to] let them slip and say, ‘well, maybe we can do that’” (Interviewee B08). While these business barriers pertain to the context innovating nano-agrifoods, they may be relevant for other areas of technological development more broadly.

4. Discussion & Conclusion

Given that food and agriculture may be among the most important sectors to ensure and demonstrate responsible innovation of nanotechnology, it is important to highlight and describe potential barriers that may exist for responsible innovation within nano-agrifood sectors. Our analysis aimed to highlight key barriers that U.S. nano-agrifood researchers working in industry and academia face to responsibly innovate.

Results from our study include a typology of barriers of enacting responsible nano-innovation in practice, within the context of agrifood sectors. These findings help identify and elucidate tensions between theoretical values inscribed within responsible innovation (including four pillars of anticipation, inclusion, reflexivity, and responsiveness) and the practical R&D within nano-agrifood sectors. In turn, these results also help highlight opportunities for areas of growth to improve practices and process of responsible innovation as they pertain to nano-agrifood sectors. We anticipate that many of the barriers identified from our study of U.S. developers may be experienced, in part or whole, by researchers in similar or related fields within other contexts and regulatory systems. We also note that the use of verbatim citations may further provide insights into how U.S. experts and developers conceptualize and consider barriers to responsible innovation in their work.

Overall, our study found that the *Lack of Data* was the most dominant perceived barrier according to nano-agrifood researchers and innovators (reported by 70% of all interviewees and comprised of 34.6% of all barrier-related excerpts). This barrier was followed by *Lack of Product Oversight* (reported by 60% of interviewees and comprised of 28.7% of excerpts) and *Need for Ensuring Marketability & Use* (reported by 60% of participant and comprised of 21.3% of all excerpts). In addition, interviewees reported on the *Need for Increased Collaboration* (mentioned by 40% of interviewees and comprised of 10.3% of excerpts) and *Lack of Adequate Training and Workforce* (reported by 30% of participants and comprised of 5.1% of excerpts). Our interviews with nano-agrifood researchers and innovators also identified three additional barriers endemic to R&D specific to start-up companies or venture businesses (i.e. "business barriers"). These included: *Lack of Access to Adequate Funding for R&D* (mentioned by 40% of interviewees, comprised 27.3% of business barrier excerpts), *Competition with Better Resourced Companies* (10% of interviewees, 6.1% of business barrier excerpts), and *Pressure from Market-based Motives* (35% of interviewees, 66.7% of business barrier excerpts).

These findings demonstrate and illuminate the breadth of challenges nano-agrifood researchers and innovators face to responsibly innovate in practice. Some barriers like those within *Lack of Data* relate to the scientific and technical demands of applied nanoscience, while other like *Lack of Training and Workforce* and *Lack of Collaboration* are more team-oriented in nature and speak to challenges navigating professional relationships, networks and collaborations. Still others like *Ensuring Marketability and Use* and *Lack of Trust* are societally based and prioritize communication needs with stakeholders and the public. Finally, *Lack of Product Oversight* poses challenges to decision-making as well as adequate connections with the concert of authorities who ultimately hold sway over product approval. While we present each of these barriers in Table 1 in the innovation phase that they are most affiliated with, the reality is that these barriers have implications across several innovation phases, emphasizing the importance of anticipation and adequate planning to mitigate these barriers in the different stages of innovation and within different contexts.

In addition to the challenges and implications of the identified barriers, we also identify opportunities to improve practices and process of responsible innovation across these innovation phases as they pertain to nano-agrifood sectors (Table 2). For example, the *Lack of Data* within Scientific & Technical R&D presents challenges to conducting nano-safety studies, developing nano-agrifood innovations, and understanding consumer and stakeholder perceptions of nano-agrifoods. However, at the same time, this challenge creates an opportunity to better incorporate anticipatory mechanisms within R&D innovation phases of nano-agrifood, such as the utilization of safety-by-design principles. As another example, the *Need for Ensuring Marketability & Use* also creates challenges within R&D to anticipate safety, beneficial use, and adoption of nano-agrifoods; while at the same time, presents an opportunity to incorporate anticipatory and inclusive mechanisms to engage stakeholders within early stages of nano-agrifood innovations. The *Lack of Product Oversight* barrier creates challenges in R&D processes, in terms of understanding and conducting adequate nano-safety studies, as well as challenges in Post-Commercialization Marketability & Use, to collect data and information on nano-agrifood products on the market and understanding the robustness of oversight mechanisms. However, these challenges also present opportunities to incorporate anticipatory mechanisms within R&D and present opportunities for researchers, innovators, and other stakeholders to monitor and evaluate oversight mechanisms post-commercialization, to better evaluate and align with principles of responsible innovation. See Table 2 for more details of highlighted challenges, opportunities, and implications of identified barriers to responsible innovation of nano-agrifoods based on outcomes from this study.

Table 2. Emergent Challenges, Opportunities, and Implications of Barriers to Responsible Innovation of Nano-Agrifoods across Innovation Phases, based on outcomes from this study. Note: Table 2 does not aim to represent all challenges, opportunities, and implications from barriers to responsible innovation of nano-agrifoods more broadly, but rather aims to illustrate important themes as they emerged from our study.

	Challenges, Opportunities, & Implications Across Innovation Phases		
Primary Barriers	**Scientific & Technical R&D**	**Product Oversight**	**Post-Commercialization Marketability & Use**
Lack of Data	• Challenges to conduct nano-safety studies • Challenges to understand and control nano-agrifood innovations • Challenges to anticipate consumer and stakeholder perceptions and acceptance of nano-agrifoods • Opportunities to incorporate anticipatory mechanisms within nano-agrifood innovations, such as safe-by-design principles	• Challenges to deal with uncertainties in regulatory risk assessments and/or approval processes • Challenges to adapt and/or develop nano-specific oversight mechanisms • Challenges to collect data and information on nano-agrifood products being developed or on market • Opportunities for researchers, innovators, and regulators to adapt current risk assessments and approval processes to align with principles of responsible innovation	• Challenges to develop nano-agrifood products that are trusted, safe and beneficial • Challenges to collect data and information on nano-agrifood products being developed or on market • Uncertainty in how stakeholders perceive and respond to nano-agrifoods • Opportunities for researchers, innovators, and other stakeholders to deal with uncertainties in post-commercialization, marketing, and use to align with principles of responsible innovation
Lack of Adequate Training & Workforce	• Challenges to attract skilled workforce to conduct R&D in nano-agrifood fields • Challenges to train researchers to develop and work with nanomaterials used in food/agriculture innovations • Opportunities to recruit and train nano-agrifood researchers and innovators to responsibly innovate	• Challenges to deal with uncertainties in regulatory risk assessments and/or approval processes • Challenges to understand and navigate nano-specific oversight mechanisms • Opportunities to recruit and train nano-agrifood researchers and innovators to communicate and collaborate with oversight and regulatory bodies to pursue responsible innovation	• Challenges to develop nano-agrifood products that are trusted, safe and beneficial • Challenges to have adequate training and workforce to monitor and navigate post-commercial marketing & use of nano-agrifoods • Opportunities to recruit and train nano-agrifood researchers and innovators to monitor and evaluate post-commercial marketing & use of nano-agrifoods
Need for Increased Collaboration	• Challenges to collaborate with outside parties to develop safe, cost-effective nano-agrifood	• Challenges of collaborating across sectors and stakeholder groups in developing regulatory risk	• Challenges of collaborating across sectors and stakeholder groups to monitor and navigate post-

	products, including increased costs • Challenges to have third-party nano-product testing, including safety studies, including increased costs • Opportunities for multi-stakeholder collaborations to anticipate, reflect upon, and respond to responsibly innovate nano-agrifoods	assessments and/or approval process • Challenges of collaborating across sectors and stakeholder groups to understand and navigate nano-specific oversight mechanisms • Opportunities to develop and/or participate in multi-stakeholder collaborations to develop responsible nano-agrifoods	commercial marketing & use of nano-agrifoods • Opportunities to develop and/or participate in multi-stakeholder collaborations to monitor and navigate post-commercial marketing & use
Lack of Product Oversight	• Challenges to understand and conduct adequate nano-safety studies • Challenges to understand and navigate upcoming regulatory risk assessments and/or approval processes • Opportunities to incorporate anticipatory mechanisms within nano-agrifood innovations, such as safe-by-design principles	• Challenges to deal with uncertainties in regulatory risk assessments and/or approval processes • Challenges to adapt and/or develop nano-specific oversight mechanisms • Challenges to collect data and information on nano-agrifood products being developed or on market • Opportunities for researchers, innovators, and regulators to adapt regulatory risk assessments, approval processes, and/or oversight mechanisms to align with principles of responsible innovation	• Challenges to oversee and regulate nano-agrifood products that are trusted, safe and beneficial • Challenges to collect data and information on nano-agrifood products on market (or soon to be) • Challenges in understanding robustness of oversight mechanisms for nano-agrifoods • Uncertainty in how stakeholders perceive and respond to nano-agrifoods • Opportunities for researchers, innovators, and other stakeholders to monitor and evaluate oversight mechanisms for in post-commercialization, marketing, and use to align with principles of responsible innovation
Need for Ensuring Marketability & Use	• Challenges to anticipate safety, beneficial use, and adoption of nano-agrofood products • Challenges to anticipate consumer and stakeholder perceptions and acceptance of nano-agrifoods • Opportunities to incorporate inclusive and/or anticipatory mechanisms within nano-agrifood innovations, such as engaging	• Challenges to understand and navigate nano-specific oversight mechanisms • Opportunities for researchers, innovators, and regulators to adapt approval processes, and/or oversight mechanisms to align with principles of responsible innovation	• Challenges to collect data and information on nano-agrifood products on market (or soon to be) • Uncertainty in how stakeholders perceive and respond to nano-agrifoods • Opportunities for researchers, innovators, and other stakeholders to deal with uncertainties in post-commercialization, marketing, and

	stakeholders and safe-by-design principles		use to align with principles of responsible innovation

In addition, the findings from our study show that there is also a need for increased inclusion and coordination of various stakeholders across different innovation phases. In fact, many scholars of responsible innovation find value in conceptualizing innovation in terms that encourage more inclusive and transparent values and processes which include stakeholder engagement earlier in innovation stages compared to standard approaches (Stilgoe et al. 2013; van de Poel, 2020). These models depart from more traditional conceptualizations of innovation which may silo stakeholder engagements into distinct dimensions within the innovation pipeline (e.g. not considering skepticism of product efficacy early in R&D). Moreover, our analysis reveals that in fact, various stakeholders can play distinct roles in concert with researchers and innovators as they navigate barriers to responsible innovation across innovation phases. For example, key stakeholders involved in R&D phases often include academic, industry, and government researchers and even potential future skilled workers (e.g. students, educators interested in nano-agrifood sectors) who can best address prescient technical challenges and who hold vested interests in broadening nano-agrifood innovations while seeking opportunities to commercialize desirable, safe, and effective products. However, even in early R&D stages of innovation, innovators may benefit from our findings to better anticipate downstream barriers and prioritize early efforts of stakeholder inclusion outside of innovators' direct institutions. To illustrate this point, noting that other nano-agrifood innovators have been challenged by the apparent lack of regulatory guidance, future innovators may seek to involve persons and agencies who serve as third-party arbiters and compliance functionaries who are tasked with regulating and guiding product developers to ensure an adequate level of safety prior to commercialization. Similarly, consumers, advocacy groups, industries, as well as academic, government, and non-profit researchers could be engaged early in R&D phases to identify barriers related to post-commercialization marketability and use while promoting values of transparency and inclusivity, also advocated by consortia and not-for-profit organizations (e.g. Center for Food Integrity (2021)) which seek to instill greater public confidence in US food systems.

In conclusion, we identify and present the first typology of barriers to responsible innovation of nano-agrifoods based on interviews with U.S.-based researchers and innovators and discuss their potential implications across innovation phases including areas of opportunities to better align with principles of responsible innovation. Our findings may help illuminate challenges that researchers and innovators face in the pursuit of responsible innovation relevant for the field of nanotechnology with relevancy for other emerging food and agricultural technologies more broadly.

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Highlights

- This study reports the first typology of barriers to responsible innovation as perceived by researchers and product developers working in nano-agrifood sectors.
- Identified 5 key barriers to responsible innovation of nano-agrifoods: *Lack of Data*, *Need for Ensuring Marketability & Use*, *Lack of Product Oversight*, *Need for Increased Collaboration*, and *Lack of Adequate Training & Workforce*.
- Elucidates tensions between theoretical values inscribed within responsible innovation (including four pillars of anticipation, inclusion, reflexivity, and responsiveness) and the practical R&D within nano-agrifood sectors.
- Identifies opportunities to improve practices and process of responsible innovation across these innovation phases as they pertain to nano-agrifood sectors.