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How can we promote the responsible innovation of nano-agrifood research?

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ABSTRACT

The use of nanotechnology and engineered nanomaterials in food and agriculture (nano-agrifoods) may provide numerous benefits to society. At the same time, there is also a chance that nano-agrifood innovations may pose new or unknown risks to human or environmental health and safety. To understand these issues and be more responsive to public concerns, researchers are beginning to discuss and adopt an emerging best practice in science and technology communities known as "responsible innovation" (RI). Originally developed by researchers over ten years ago, RI is now a well-established framework that is already a part of science policy-making in the European Union (as "responsible research and innovation"). In the United States, however, there are numerous structural and institutional barriers for scientists to align their research with RI principles and goals. This perspective briefly reviews RI, why it is needed for nano-agrifoods, and how it could be institutionalized more effectively in the U.S. to ensure that future nano-agrifood research is better aligned with societal needs, expectations, and concerns. This work also identifies several pathways to institutionalize RI in nano-agrifoods, ranging from a public legal mandate to privately enforced organizational norms. Further, a set of strategies and/or best practices for implementing RI in the U.S. context is presented that are applicable to both public and private organizations. While key findings from this work are focused on the need for RI of nano-agrifoods in the U.S., implementation of these best practices could have positive benefits for other emerging technologies and in other national contexts as well.

1. Introduction

The use of nanotechnology and engineered nanomaterials in food and agriculture (nano-agrifoods) may provide numerous benefits to society. For example, nano-fertilizers and nano-pesticides aim to improve the delivery of agrochemicals while reducing environmental runoff (Sampathkumar et al., 2020). Other innovations and products have used engineered nanomaterials to enhance the nutritional value of foods or improve the absorption of dietary supplements (Nile Shivraj et al., 2020; Prakash et al., 2018). Nano-vaccines for livestock have been developed to deliver more animal-friendly veterinary medicine (Renu et al., 2020).

At the same time, like other emerging technologies, there is also a chance that nano-agrifood innovations may pose new or unknown risks to human or environmental health and safety (Grieger et al., 2016a; 2016b; McClements et al., 2017; Grieger et al., 2019; Li et al., 2019; Cummings et al., 2021). However, not all nano-agrifoods may present the same degree of risk or offer the same level of benefit. Some applications may have clearer benefits and align with societal needs, such as nano-fertilizers that have more efficient nutrient delivery and decreased environmental runoff compared to conventional fertilizers (Sampathkumar et al., 2020). Decreased nutrient runoff may be particularly attractive, given the role of agricultural fertilizer runoff in decreasing water quality and increasing rates of eutrophication and harmful algal blooms (USGS, 2019; NRC, 2009). Other nano-agrifood applications may have unclear benefits to society or to consumers while also introducing numerous uncertainties in terms of impacts on health and the environment (Okeke et al., 2022). For example, the impacts of nano-scale dietary supplements (e.g. nano-Cu, nano-Ag) and nano-scale food color additives (e.g. nano-TiO2) are still under investigation in many cases (Cholewińska et al., 2018; Winkler et al., 2018; Baranowska-Wójcik et al., 2020). The European Food Safety Authority (EFSA) has, in fact, recently declared that food grade TiO2 (E171) is no longer considered safe as a food additive, largely in part due to genotoxicity studies involving TiO2 nanoparticles (EFSA, 2021). Other benefit-risk ratios apply to a range of other nano-agrifood products,

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including those in late stage R&D or currently on the market (Okeke et al., 2022).

In the U.S., existing rules and regulations require that for most products, researchers must conduct safety studies in order to obtain approval and market nano-agrifood products.[1] While this is essential to protecting environmental, health, and safety (EHS) impacts and to help ensure trust among developers, regulators, and consumers, there are no institutional requirements or expectations for these researchers to conduct studies to understand societal and ethical implications of their new, nano-enabled products, including engagement of diverse publics and consumers to understand their concerns and desires with regard to the technologies. Too often, the existing scholarly literature on stakeholder perceptions is divorced from the actual practices of nano-agrifood research and innovation. In many cases, researchers may not obtain funds or support for public perception studies until the marketing stage, after the product is already developed and approved by regulators. This is problematic, because if researchers fail to understand public perceptions and concerns about nanotechnology in food and agriculture prior to finalizing or marketing their product, it is possible that researchers may develop products that consumers do not believe are useful, necessary, or even safe (Gupta et al., 2015). Overall, without greater transparency, assurance of safety, and better public understanding of nanotechnology, long-term consumer trust in agrifood nano products could be in jeopardy.

To understand these issues and be more responsive to public concerns, researchers are beginning to discuss and adopt an emerging 'best practice' in science and technology communities known as "responsible innovation" (RI). RI has been incorporated into science and technology policy in the European Union, to mixed success (Owen, 2021, Shelley-Egan et al., 2018). However, in the United States, there are numerous structural and institutional barriers for scientists to align their research with RI principles and goals (Kuzma and Roberts, 2018; Roberts et al., 2020; Wittrock et al., 2021; Grieger et al., 2022). Among other barriers, taking additional steps to anticipate potential impacts, engage stakeholders, and respond to feedback, can significantly delay or even halt the research and development of new products (Cummings et al., 2021). Thus, it is especially important to "*institutionalize*" RI so that researchers whose work is aligned with RI are not placed at a competitive or funding disadvantage (Wittrock et al., 2021).

In this perspective, the main concepts of RI are reviewed, along with highlights of why RI is needed for nano-agrifoods, and how it could be institutionalized effectively in the U.S. to ensure that future nano-agrifood research is better aligned with societal needs, expectations, and concerns. This perspective also presents several policy options that may be considered, including the possibility of mandating RI for all publicly funded research. More broadly, this work also offers a set of strategies and/or best practices for implementing RI in the U.S. context that are applicable to both public and private organizations.

2. What is responsible innovation (RI)?

RI is an approach developed by scholars to better align research and innovation with societal needs and expectations to create sustainable, equitable, and just outcomes compared to traditional innovation models. Often described as "taking care of the future through collective stewardship of science and innovation in the present," one highly cited and utilized version of the framework includes four "pillars" - anticipation, reflexivity, inclusion, and responsiveness (Stilgoe et al., 2013). For instance:

- Early-stage research activities should include efforts to **anticipate** future impacts.
- To ensure their work aligns with societal expectations, norms, and preferences, researchers should open an **inclusive** dialogue with a range of actors.
- Innovators and researchers should then **reflect** on their motivations and assumptions.
- Innovators and researchers should then **respond** to feedback from stakeholders, anticipatory activities, and their own reflection, and make changes accordingly.

Scholars have suggested that additional principles, such as transparency (Kuzma and Grieger, 2020), sustainability, and care (Burget et al., 2017), should also be included. Critics point out that RI is not politically neutral (van Oudheusden, 2014) and the focus on 'innovation' is too aligned with pro-growth economic policies (De Saille et al., 2020). Nevertheless, the authors find that RI has clear potential to generate cross-sector coalitions among existing actors in innovation systems (Kuzma and Cummings, 2021; Roberts et al., 2020) that could lead to transformational change.

3. Why is RI needed for nano-agrifood research in the United States?

RI is needed for nano-agrifood research because the risks and benefits of novel products created with nanotechnology are not always certain, and there are few formal pathways to include the perspectives and voices of various publics and stakeholders in existing innovation systems. Numerous studies show that the general public regards nanotechnology in food and agricultural applications more favorably than biotechnology applications like genetic engineering, although perceptions depend on the product or application (Yue et al., 2015a, 2015b). It is also known that consumers want to know what is in their food supply, and have transparent and clear information on if and how nanotechnology is used in food and agricultural products (Brown and Kuzma, 2013; Chuah et al., 2018; Porcari et al., 2019). In fact, foods in Europe that contain nanotechnology or engineered nanomaterials are now required to be labeled to indicate the presence of nano-scale ingredients, since December 2014 (European Commission, 2014). While U.S. agencies have promulgated guidance for industry (e.g. EPA, 2017, FDA, 2014), no comparable mandatory provisions currently exist in the U.S. (Grieger et al., 2016a). Overall, by taking additional measures to anticipate new risks, engage stakeholders early in the innovation process, and respond to feedback and/or new information, researchers and innovators can respond to potential concerns well before they are tried in the court of public opinion.

In a recent stakeholder engagement study, our team found that stakeholder participant concerns about nano-agrifoods were largely centered around evaluations of safety and risks (Grieger et al., 2021). Participants also expressed a clear preference for products that responded to a meaningful societal need or demonstrated clear benefits, and they opposed the development of products where the need was less clear or the benefits did not outweigh potential risks. Participants in our study favored action by government agencies as well as private companies to ensure that their innovations were responsible and that the development of unsafe new products was prohibited. These findings suggest that researchers and innovators should continue to pay attention to the environmental, health, and safety risks of nano-agrifoods, and acknowledge that stakeholders have expressed support for more oversight of nano-agrifood innovation (Grieger et al., 2021).

Finally, there is a valuable opportunity for policymakers to learn from other efforts to implement RI principles elsewhere. For example, the European Commission has incorporated a version of RI, "responsible research and innovation," (RRI) into the Horizon 2020 initiative. The EU experience reveals that RI is most effective as a policy tool when it remains a "site for ongoing debate" rather than a fixed standard (Owen et al., 2021).

[1] A notable exception is dietary supplements. See: Dietary Supplement Health and Education Act, Pub. L. No. 103–417, 108 Stat. 4325 (1994).

4. What are some pathways to institutionalize RI for nano-agrifood research in the United States?

Below, three pathways to institutionalize RI are described that range from fully private (RI as organizational norm) to fully public (new laws or regulations to promote RI). In the middle, suggestions for mandating RI for publicly funded research are presented, which would necessarily involve some coordination between public and private entities. These suggestions focus on breaking down what Wittrock et al. (2021) describe as cultural, structural, and interchange-related barriers to RI. These pathways can also be understood in terms of a macro- (national), meso- (organizational), and micro- (individual) level, following Kuzma and Roberts (2018).

4.1. Establish RI as a private organizational norm

Currently, RI is largely implemented by U.S. researchers on an individual, project-by-project basis. This is because there are no mandates or institutional requirements to follow RI practices within organizations, beyond the conduction of safety studies or guidelines to conduct research in ethical ways (e.g. Collaborative Institutional Training Initiative (CITI) certification, Institutional Review Boards (IRB) approvals). In the absence of public mandates, RI could be implemented at the level of individual organizations or private companies. For privately funded research, organizations who conduct or sponsor research could evaluate how RI fits into their existing organizational culture, and develop processes and procedures to encourage their researchers to align their work with RI principles (Wittrock et al., 2021). Over time, RI could be gradually normalized as part of the everyday practices and protocols of research at individual organizations (Grieger et al., 2022).

There are several models that could be used to implement this approach. For example, the way an organization implements RI could be modeled after how the organization already enforces norms for research ethics, scientific integrity protocols, and conflicts of interest management. While it is important to note that RI is not the same as research ethics and would not supplant existing research ethics protocols, its implementation within organizations could nevertheless follow similar pathways, or use similar platforms for compliance. This strategy could gradually ease researchers and innovators into thinking about RI alongside other best practices in research.

A more formalized and coordinated approach could involve guidance from international standard-setting organizations, such as the International Organization for Standardization (ISO). These "voluntary consensus" approaches have historically been effective in other areas, such as engineering and electronics, and tend to be more responsive and adaptive than standards set by domestic regulatory agencies or legislative bodies (Yates and Murphy, 2019; Murphy and Yates, 2009).

4.2. Mandate RI for federally funded research

Even if individual organizations adopt RI, without some kind of external enforcement mechanism, many of the current institutional and structural barriers to RI will likely remain. It is here that additional incentive structures may be needed to accompany any processes of implementation of RI at the organizational level. One key incentive would be greater access to the financial resources to pursue additional activities related to RI. This could involve public funding as well as venture capital flows to researchers who prioritize RI, or a combination of public and private coordination through cooperative governance (Jordan et al., 2017).

In particular, federal grant-making agencies can provide a crucial link between RI implementation at the meso (organizational) level and the macro (national) level, by adjusting public funding priorities to encourage alignment with RI (Kuzma and Roberts, 2018). While funding agencies could act much more swiftly and decisively if directly supported by Congress or the Executive Branch, these agencies have some flexibility to adjust priorities in coordination with the National Science Board, Congress, and the Office of Science and Technology Policy (NRC, 2004).

Ideally, these agencies could require alignment with RI as a condition of receiving federal research funds for all projects related to nano-agrifoods. For example, federal grant applications could require researchers to develop a plan for how they will fulfill the RI principles in their work. These plans would be approved at the application stage, before funds are awarded. The process of developing and approving an RI "plan" could be modeled on other management-based regulatory approaches, in which agencies would not prescribe how to implement RI, but they could provide a range of examples or models from which researchers could develop a plan tailored to their specific research project (Coglianese and Lazer, 2003). Enforcement would likely involve periodic audits or reviews, which could be incorporated into existing auditing and planning processes for federal grants.

However, because RI has a broader scope than that of most regulatory agencies, it might be challenging or infeasible for agencies to formally mandate RI without explicit legislative or executive authorization. Without explicit access to the resources and capacity to do so, agencies would have minimal authority to oversee privately funded research. However, as the agencies develop the necessary monitoring and enforcement capacity to ensure that federally funded research aligns with RI, it is plausible that the expertise developed in that process could then be used in the private sector as well.

4.3. New laws, regulations, or Executive Orders defining RI

A more decisive implementation of RI could be achieved at the macro-level through a public mandate and/or appropriation of public funds explicitly for this purpose. The U.S. Congress and/or the Executive Branch could take actions to codify RI through law, empower regulatory agencies to enforce it, and/or mandate its inclusion in future publicly funded research. For example, a new statute that defines RI, an Executive Order that explicitly states that RI is an executive priority or formal rulemaking to define RI on an agency-by-agency basis could all clarify the importance of RI in a very public way.

These policy options could be very effective, but also pose significant challenges. First, a legislative or executive mandate would necessitate that funding agencies become enforcers. This might prove especially challenging for those agencies, as RI explicitly demands consideration of public inclusion, anticipation of risks and benefits at very early stages of innovation, and responsiveness to public hopes and concerns, well before regulatory agencies typically intervene. Secondly, nano-agrifoods have such a wide range of potential uses and applications, many of which are still in development and evolving. Unless a law is written in a very open-ended way, it could undermine the very flexibility that is a core strength of the RI principles, and eventually lose relevance as the technology matures. Third, it is worth noting that in the current polarized political environment, any involvement by the Executive Branch or Congress risks introducing the ideas of RI into a contentious political space. As Wittrock et al. (2021) note, there is a not-insignificant danger of RI becoming associated with a particular political party in these contexts.

Even if RI were clearly defined by Congress or the Executive Branch, that definition would have to be accompanied by funding through appropriations to generate lasting change. Given that researchers frequently cite the cost of RI as a barrier, it is unlikely that funding agencies would have the capacity to monitor or enforce compliance with RI without additional resources. However, setting out a clear definition of RI without additional resources might be beneficial if it gave agencies discretion to build capacity for monitoring and enforcement as a longer-term goal.

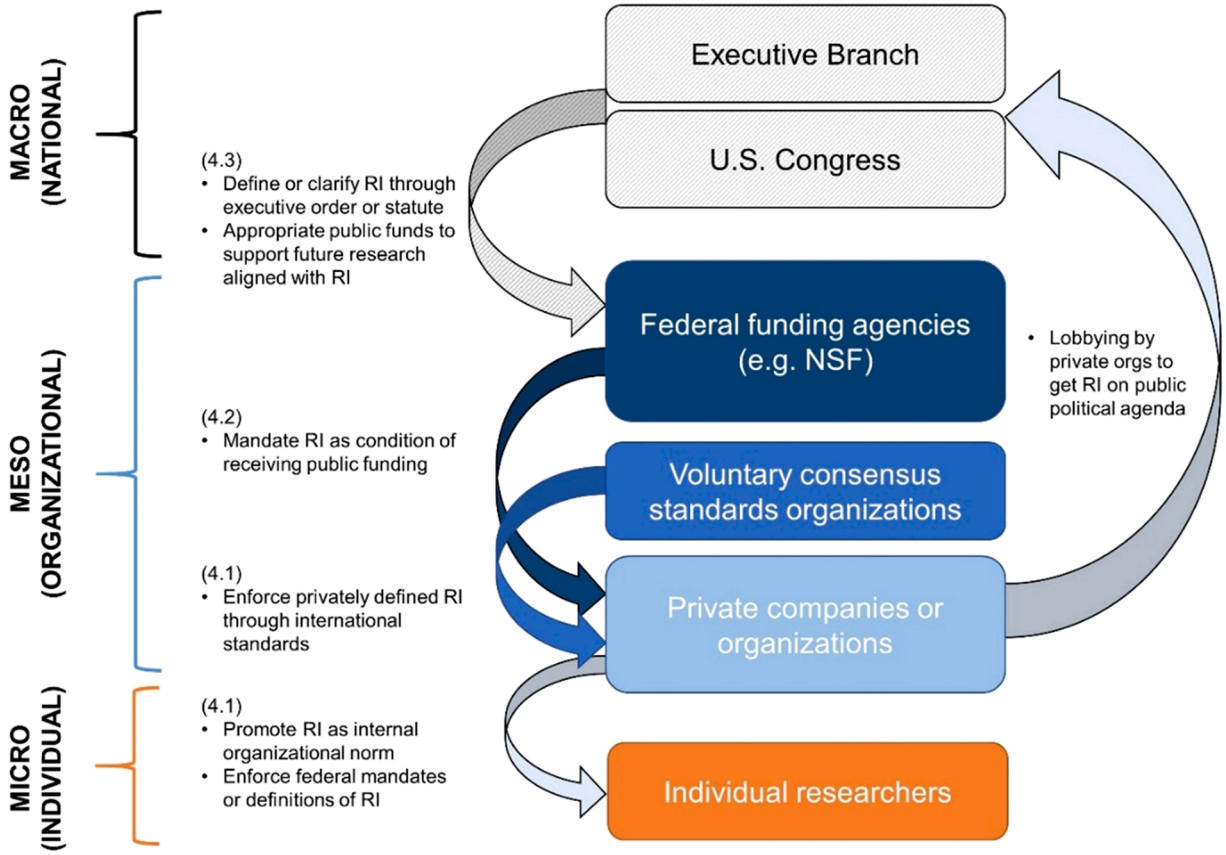

Fig. 1. Illustration of how different pathways can exert influence over different actors to institutionalize RI in the US context. Micro, meso, and macro framing drawn from Kuzma and Roberts (2018); Kuzma (2022)– in review.

4.4. Combination of public and private pathways to institutionalize RI

While each of these pathways could be pursued independently, in practice, they may be co-dependent on one another (Fig. 1). For example, private organizations may be far more likely to earmark internal resources to support RI if doing so will improve their competitiveness for public funding. Similarly, funding agencies could gradually shift their priorities to align with RI even without backing by Congress or the Executive Branch, but even the most cursory lip service in the form of an Executive Order (EO) or a statement of legislative priorities would significantly strengthen funding agencies' position in this regard. Appropriations from Congress would greatly accelerate funding agencies' capacity to align future research with RI while simultaneously attracting the interest of private organizations. Conversely, the U.S. Congress or Executive Branch might have greater political incentive to act on RI if private organizations initiated interest in the issue. Private organizations would be more likely to lobby for implementation of RI in publicly funded research if they had already adopted some of its principles, and it provided them with some advantages over their competitors, i.e. to "raise rival's costs" (Salop and Scheffman, 1983).

5. What are some considerations to ensure effective institutionalization of RI for nano-agrifood research in the United States?

Regardless of how RI is implemented, the following considerations will be important to effectively institutionalize RI as a best practice in U.S. nano-agrifood research.

5.1. Priority-setting to manage time and resources

Some research projects or potential nano-agrifood products may present greater uncertainties or pose greater potential risks or societal concerns than others; these projects or products should be given more attention and analysis than products whose risks or potential concerns may be lower (Grieger et al., 2022). Ideally, definitions, statutes, or formal policy statements about RI should include language that will enable this kind of flexible, tiered approach.

Within organizations, screening processes can help researchers identify higher-risk products that may require additional scrutiny, while managing time and resources efficiently. Initially, implementing these processes may require additional funding or other support, including hiring of new staff specifically trained in risk assessment and risk screening techniques. Over time, such expertise will gradually become internalized within organizations, funding agencies, or research teams.

5.2. Incentives to promote education and compliance

In their efforts to institutionalize RI, agencies and organizations may want to focus on creating incentives ('carrots') rather than imposing penalties ('sticks'). For example, organizations could earmark additional funding or research support for projects that demonstrate a commitment to the goals of RI. That funding could then be used to hire RI practitioners to conduct stakeholder engagement work, or to support additional risk assessment at early stages of research. Funding agencies require budgets and grant proposals to include specific line items to account for the cost, time, and expertise needed to conduct RI-aligned work.

Recent research shows that lack of awareness or understanding of RI among scientists themselves is a major barrier to its implementation

(Cummings et al., 2021). To overcome this problem, organizations could incorporate RI into responsible conduct of research training or other continuing education modules, to encourage both experienced PIs and new researchers alike to learn more about RI. Similarly, funders could implement RI-specific training as part of required training for federally funded research.

A more long-term approach could involve partnerships between universities and funding agencies to design graduate programs tailored around building the expertise and skills needed to successfully conduct research aligned with RI. One comparable model is NC State University's NSF-funded AgBioFEWS program, in which students "examine the science, policy, and public engagement aspects and impacts of agricultural biotechnology" through multidisciplinary graduate training.[2]

5.3. Monitoring to encourage continuous improvement

Regardless of whether RI is implemented through public or private measures, it is crucial to establish clear processes of monitoring and review to ensure that policies, procedures, and incentives to institutionalize RI are having the intended effect. For example, internal and external audits, progress reports, and other forms of peer review could ensure that researchers are adhering to the principles of RI. Funding agencies might ask researchers to include statements on how they used grant funds to align their work with RI as part of their annual reporting requirements. These systems for monitoring and review can also provide crucial information to encourage further policy learning going forward and iteratively improve organizational practices for RI education and training.

6. Conclusion

In order to realize the potential benefits of nanotechnology in food and agriculture, it is imperative that researchers attend to the social and ethical dimensions of innovation. Researchers who follow the principles of responsible innovation (RI) are better equipped to address public concerns before new products reach the marketplace, and minimize the degree of controversy or backlash compared to other new technologies.

In this perspective, several pathways to institutionalize RI in nano-agrifoods are considered. These include pathways situated at the individual (micro), organization (meso), and national (macro) levels, and range from promoting RI as internal organization norms and developing standards for RI in research, to mandating RI as a condition to receive public funding, to developing executive orders or statutes to support RI research. In addition to describing these three distinct pathways, this perspective also illustrates how they are co-dependent on one another to fully implement RI in both public and privately funded nano-agrifood innovation. This perspective concludes by describing a set of common strategies to establish RI as a best practice that would be relevant for any combination of public and private enforcement. Key findings from this work may strengthen research and innovation of nano-agrifoods in the U.S. as well as other emerging food and agricultural technologies as well.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

[2] AgBioFEWS: Agricultural Biotechnology In Our Evolving Food, Energy, and Water Systems. NC State Genetic Engineering and Society Center. https://research.ncsu.edu/ges/academics/agbiofews/.

Data Availability

No data was used for the research described in the article.

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