NOVEL AND EXCEPTIONAL TECHNOLOGY AND RESEARCH ADVISORY COMMITTEE

Draft Report of the Working Group to Establish a NExTRAC Framework

NATIONAL INSTITUTES OF HEALTH
Novel and Exceptional Technology and Research Advisory Committee (NExTRAC)

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NATIONAL INSTITUTES OF HEALTH

Novel and Exceptional Technology and Research Advisory Committee (NExTRAC)

Working Group to Establish a NExTRAC Framework

Draft Framework WG Report

I. Introduction

The purpose of the NExTRAC, as noted in the committee's charter, is to "provide advice to the Director, National Institutes of Health (NIH), on matters related to the conduct and oversight of research involving emerging technologies in biomedical science (also referred to as emerging biotechnologies)... The Committee will address scientific, safety, ethical, and social issues associated with areas of emerging biotechnology research for which the NIH requests advice or guidance." To launch the work of the committee, the NIH Director established the Working Group to Establish a NExTRAC Framework, providing the following charge:

- "Describe effective approaches for prospectively identifying emerging biotechnologies or specific applications with reasonable potential to have important scientific, safety, or ethical considerations

- Conceptualize a framework for NExTRAC deliberation of issues surrounding emerging biotechnologies and applications, including:
  - Guiding principles for when an emerging biotechnology or its applications would significantly benefit from further public deliberation
  - A potential process by which the NExTRAC will consider or evaluate any given emerging biotechnology or its applications

- The working group will consider
  - Applications of emerging biotechnologies, given that the way the biotechnology is used often generates the safety, social, or ethical issues
  - Effective horizon scanning approaches; focusing on biotechnologies and applications that are reasonably anticipated vs. hypothetical
  - Cross-cutting issues that may be relevant for a variety of emerging biotechnologies and applications
  - Strategies for committee engagement and soliciting feedback"

The framework, including the description of effective approaches for horizon scanning, will assist the NIH Director in identifying emerging biotechnologies and applications with reasonable potential to have important scientific, safety, or ethical considerations within the NIH mission. The working group was not asked to identify specific issues or priorities for the NExTRAC, but

instead to provide guidance on effective approaches NIH might use to scan the horizon and guiding principles NIH may consider when determining if a specific issue merits public deliberation by the committee. This framework will help inform the NIH Director as he or she considers which topics and tasks merit the attention of the committee. Additionally, the framework will be an effective tool for the committee itself when considering any given charge provided by the NIH Director. We hope this report may also be a useful product for the broader community including different arms of the US Government as well as non-governmental advisory bodies that may also be considering what emerging biotechnologies and applications merit special attention, and what the process for deliberation should look like. Ultimately, this draft report, a product of the working group, will be considered by the NExTRAC for public deliberation.

II. Prospective Identification of Biotechnologies and Applications

The first part of the working group's charge was to "describe effective approaches for prospectively identifying emerging biotechnologies or specific applications with reasonable potential to have important scientific, safety, or ethical considerations." The working group considered the "prospective identification" of emerging technologies or applications to be similar to what is commonly referred to as "horizon scanning," and so the working group considered existing approaches to horizon scanning and lessons learned to formulate components of an approach for such efforts, for consideration by the committee and, ultimately, NIH.

A. General Aspects of Horizon Scanning

There are a number of approaches described in the literature related to scanning the horizon for emerging areas of research and technologies. The underlying purpose of all of these approaches is to prospectively identify emerging and innovative areas in early stages of development. Prospective identification allows policy-makers, scientists, and industries to plan for the future in a proactive manner.

There is no perfect method of identifying developing areas of research and related technologies, and exact methodologies and inputs into such exercises vary based on the purpose of the scan. However, several components common across previous efforts can inform effective approaches for NIH to consider employing in prospective identification of emerging biotechnologies or specific applications with reasonable potential to have important scientific, safety, or ethical considerations. The working group notes that there may be overlaps in scientific, safety, and ethical considerations. Safety issues, for example, often have scientific considerations, and safety itself can be considered an ethical issue.

Though the steps described in methodologies vary somewhat by approach, the essential components of horizon scanning outlined in the literature are similar. In a meta-analysis of horizon scanning methodologies, Hines et al.[1] categorize the basic steps as:

1. signal identification and detection,
2. criteria and methods of filtration and prioritization,
3. assessment, dissemination and updating of information, and
4. overall evaluation of the process

Signal detection in the context of horizon scanning is the process by which early signs of

[1] Hines, P., Hiu Yu, L., Guy, R. H., Brand, A., & Papaluca-Amati, M. Scanning the horizon: A systematic literature review of methodologies. *BMJ Open* **9(5)**, e026764 (2019).

potentially important developments are identified. Signal detection and filtration methodologies can be qualitative or quantitative in their approaches. For example, filtration methods could be based on automated text mining tools or expert participation. Many horizon scanning approaches use a mixture of qualitative and quantitative research methods.

Some of the key considerations when determining which technologies are likely to emerge and have a significant impact include comparisons with existing technologies and applications. For example, whether the technology is innovative and significantly different from other technologies, and whether it is in development for many applications, may give insight into the potential impacts. In addition, if there are multiple other applications for the same technology, considering the impacts of different applications can inform whether the emerging technology is likely to be particularly disruptive.

B. Lessons Learned from Previous Horizon Scanning Efforts

Previous horizon scanning efforts have strengths and weaknesses for the purposes of the charge to this working group, and the appropriateness of a particular model is related to the ultimate purpose or application of that model.

In general, effective horizon scanning approaches have:

- Varied methods and sources for signal detection
- Well-defined scope
- Specified timeframes that are aligned with the goals of the horizon scanning and the end uses
- Clear and relevant criteria for prioritization of scanning results
- Diverse groups of experts contributing to horizon scanning processes
- Explicit, integrated ways of identifying and mitigating potential sources of bias and psychological heuristics
- Options for evaluating the effectiveness of the scan

For the purpose of the working group and NIH, “horizon scanning” may be considered to mean an approach or approaches for identifying emerging technologies or applications with reasonable potential to have important scientific, safety, or ethical considerations within the NIH mission space. Then, NIH may utilize a set of prompts for when a technology or application would significantly benefit from further deliberation by the committee. Given this focus, some previous horizon scanning efforts are less applicable, for various reasons. For example, in some cases, the definition of biotechnology would be too broad or narrow for the NIH mission space, or there may be too much focus on technologies with known impacts.

i. Information sources and techniques for filtering

Previous horizon scanning efforts have used a wide variety of information sources for detecting signals. Commonly, the scientific literature is used to identify novel and innovative technologies. Other sources traditionally include searches of patents and patent applications, inputs from industry and funders, expert input from individuals or groups, surveys, government bodies, meetings and conferences, grey literature, previous horizon scanning efforts, international institutions, and other inputs such as clinical trials databases. They may also include more nontraditional sources such as media (including journalism, art, literature, and pop culture

content), social media, and preprints available on prepublication servers.[2,3] The most effective sources of information and filtering for the purpose of the charge to this committee are outlined in the following table.

Table 1. Effective Sources of Information and Filtering.

	Types	Consideration(s)
Sources	Highly flexible and uses a variety of credible sources of information	Confirmation of reliability of information sources when possible.
	Diverse set of voices	
Filtering Techniques	Quantitative approaches (e.g., portfolio analysis tools)	• For quantitative approaches, human input may be needed particularly at the filtering stage. • Identification of the appropriate pipeline for gathering input from different sources. • Identification of appropriate criteria and methodology for filtering.
	Qualitative approaches (e.g., workshops)	

Information sources should be variable and credible, including both primary and secondary sources. In addition, a diverse set of voices should be incorporated including experts from multiple disciplines (e.g., scientists, ethicists, venture capitalists, advocacy groups, public(s)) and experts of variable age and experience (e.g., principal investigators, post-doctoral students, graduate students). Information sources should also incorporate diversity in gender, race, and socioeconomic status.

C. Desired Components of NIH Approach(es) to Prospectively Identify Emerging Biotechnologies or Specific Applications

There is a great deal of difficulty in predicting which biotechnologies and applications are likely to "emerge." Government bodies, venture capitalists, and scientists have attempted to do so over many years, and there is no perfect or canonical model. Indeed, because different approaches are more appropriate depending on the ultimate purpose of the scan, and to make sure diverse sources of input are captured, multiple models are likely needed that address different needs and circumstances. Outlined below are components that should be considered to achieve NIH's goal of finding the most effective approaches for prospectively identifying emerging biotechnologies or specific applications with reasonable potential to have important scientific, safety, or ethical considerations.

[2] Hines, P., Hiu Yu, L., Guy, R. H., Brand, A., & Papaluca-Amati, M. Scanning the horizon: A systematic literature review of methodologies. *BMJ Open* **9(5)**, e026764 (2019).
[3] National Academies of Sciences, E., and Medicine. Safeguarding the Bioeconomy. (The National Academies Press, 2020).

Table 2. Desired Components of NIH Approach(es) to Prospectively Identify Emerging Biotechnologies or Specific Applications

	Components
The horizon scanning focuses on and identifies…	…emerging biotechnologies and applications that fall within or are related to the NIH mission space.
	…input from diverse groups.
	…"convergence" (i.e., when technologies that were previously separate or distinct begin to align) as a harbinger of an emerging biotechnology or application.
	…early indicators of issues that would require an NIH response.
The horizon scanning process…	…integrates and builds on previous work of others to detect emerging technologies/research and gaps.
	…is iterative.
	…includes both (1) continuous horizon-scanning processes in strategically important areas and (2) stand-alone projects/processes designed to answer explicit questions.
	…includes explicit and deliberate strategies for recognizing and mitigating the effects of biases and psychological heuristics.
	…appreciates time frame appropriately tied to the purpose (likely 5-10 years).
	…has periodic re-evaluation of approaches to identify weak spots and gaps.

Relevant technologies and applications will include those that overlap and interface with the NIH's sphere, such as artificial intelligence (AI) used specifically in biomedical research. The scope of horizon scanning is not necessarily limited to NIH-funded emerging biotechnology research but would align with the NIH mission. In terms of the appropriate time frame, key questions include how long until an important impact is anticipated to occur, and, in some cases, when the technology is likely to enter clinical trials or the healthcare system. A wide range of groups should be involved in horizon scanning, including contributors from a variety of backgrounds, such as different generations and age groups, venture capitalists, advocates, and people of different genders, races, socioeconomic status, and experts from a variety of disciplines. The NExTRAC is one valuable source for ideas, suggestions, and recommendations for emerging biotechnologies and applications with a reasonable potential to have important scientific, safety, or ethical considerations. The working group encourages the NIH Director to use the NExTRAC as an active source of horizon scanning and as a sounding board for helping to identify and prioritize issues that the NExTRAC might address as it provides advice and guidance to the Director.

Both qualitative and quantitative approaches (or a combination) may be used to achieve NIH's goals. As Hines et al.[4] describe in their meta-analysis of horizon scanning efforts, "the majority of the methods used were manual or semiautomated, with relatively few automated aspects. This could be due to the limited availability of software and budget constraints. Complex filtration, prioritization and assessment criteria are some of the barriers to full automation that may be resolved in the not-too-distant future by the rapidly evolving fields of machine learning and artificial intelligence." Given the state of the science, fully quantitative tools and models to detect emerging technologies are not developed enough on their own to be suitable for the purpose of the charge to this working group. Most existing quantitative tools rely more on specific retrospective queries, rather than network analyses that would detect emerging trends in the scientific landscape that are not specific to a topic area. However, NIH should continue to track and support ongoing research at NIH and elsewhere to develop automated tools and integrate them when appropriate.

Quantitative tools can be used alongside qualitative efforts and could be brought in more systematically over time as research and development move forward and methodologies improve. Qualitative approaches currently used by NIH that can be effective for prospective identification of emerging biotechnologies and applications include workshops, town halls, and other expert engagement; working groups and committees, including public in-depth discussion and deliberations of Federal Advisory Committees; and Requests for Information. A major source of such qualitative input may arise from the deliberations and perspectives of the NExTRAC, which will in turn inform NIH's considerations of issues that would benefit from the advice of the committee and public discussion.

III. Framework for NExTRAC Deliberation

The second part of the charge to the working group was to prepare a conceptual "framework for NExTRAC deliberation of issues surrounding emerging biotechnologies and applications, including guiding principles for when an emerging biotechnology or its applications would significantly benefit from further public deliberation" and "a potential process by which the NExTRAC will consider or evaluate any given emerging biotechnology or its applications." Building upon lessons learned from other horizon scanning efforts and the development of approaches for NIH to prospectively identify relevant biotechnologies and applications that may raise important scientific, safety, or ethical considerations, some filtering must occur to guide when such matters would significantly benefit from discussion by the NExTRAC. As a first step to guide NIH's decision making, the working group identified circumstances in which an emerging biotechnology or its applications would significantly benefit from further public deliberation.

The working group also put together a potential process for NExTRAC consideration or evaluation of emerging biotechnologies or applications. The proposed process is intended to provide a flexible framework for future NExTRAC consideration or evaluation that can be applied in a charge-specific manner. The framework, and in particular the "potential process by which the NExTRAC will consider or evaluate any given emerging biotechnology or its applications" will also be a useful tool for NExTRAC consideration of any future charges given to the committee by the NIH Director.

A. When an Emerging Biotechnology or its Applications Would Significantly

[4] Hines, P., Hiu Yu, L., Guy, R. H., Brand, A., & Papaluca-Amati, M. Scanning the horizon: A systematic literature review of methodologies. *BMJ Open* **9(5)**, e026764 (2019).

Benefit from Further Public Deliberation

The working group developed the following framework for NExTRAC deliberation of issues surrounding emerging biotechnologies and applications. It is intended to address when an emerging biotechnology or its applications would significantly benefit from further public deliberation. The working group acknowledges that, given its wide breadth, this framework might suggest a broader aperture than what is ultimately addressed by the NExTRAC. We have nonetheless proposed a set of prompts for public deliberation to help inform the NIH Director as he or she considers which topics and tasks merit the attention of the committee.

The working group notes that public deliberation can have many purposes, including broadening the framing of public debate related to emerging biotechnologies and increasing transparency of public policy decisions. An inclusive process can contribute to more just and accountable analyses, conclusions, and policy decisions.[5] Thus, public deliberation can have intrinsic value, to the extent that it promotes greater public awareness and engagement, particularly in circumstances where there have historically been issues of exclusion, distrust, or lack of transparency between governing institutions and the public. That point noted, some topics may benefit more from public deliberation than others. Technologies or applications that necessitate weighing of competing values, especially about what is a public good, are particularly well-suited for public deliberation. Furthermore, technological experts who are most aware of the potential of emerging technologies might not be experts on the range of risks, benefits, or other impacts that biotechnologies might have on various populations, as defined by those populations. In some situations, public deliberation could be necessary to identify potential technological impacts, including the range of values attached to them. Finally, technologies and applications where there is greater uncertainty about the impacts or how to assess them could also benefit more from broader discussion.

Therefore, the working group identified a set of features of biotechnologies and their applications to serve as "prompts" for public deliberation. In the charge to the working group, we were asked to develop "guiding principles," but it became clear that an attempt to articulate such principles would substantially overlap with existing scientific, safety and bioethical principles. These prompts are meant to bridge the gap to such principles, which still apply to this framework and include relevance and timeliness, oversight and transparency, nonmaleficence and justice, safety and risk management, equity and justice, fairness, and autonomy and respect for personhood. The prompts are not meant to be all encompassing or in priority order, and they are not intended to be used as a checklist. In fact, a truly novel issue could arise falling within the scope of just one or two of the following prompts, and still be a high priority for discussion. In other circumstances, a biotechnology may not warrant public deliberation unless many or all are satisfied. Similarly, a biotechnology or application may raise a number of issues that may warrant public discussion, or a single simple issue may merit such discourse. These prompts can be linked to the scientific, safety and bioethical principles in Table 3.

The working group recognizes that some emerging biotechnologies and applications may merit public discourse, but this deliberation would be best conducted by entities besides the NExTRAC. As such, in conjunction with these prompts, the working group notes that any emerging biotechnology or application brought for public deliberation by the NExTRAC will fall within the scope of the NIH mission to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability. The working group further acknowledges that, in thinking

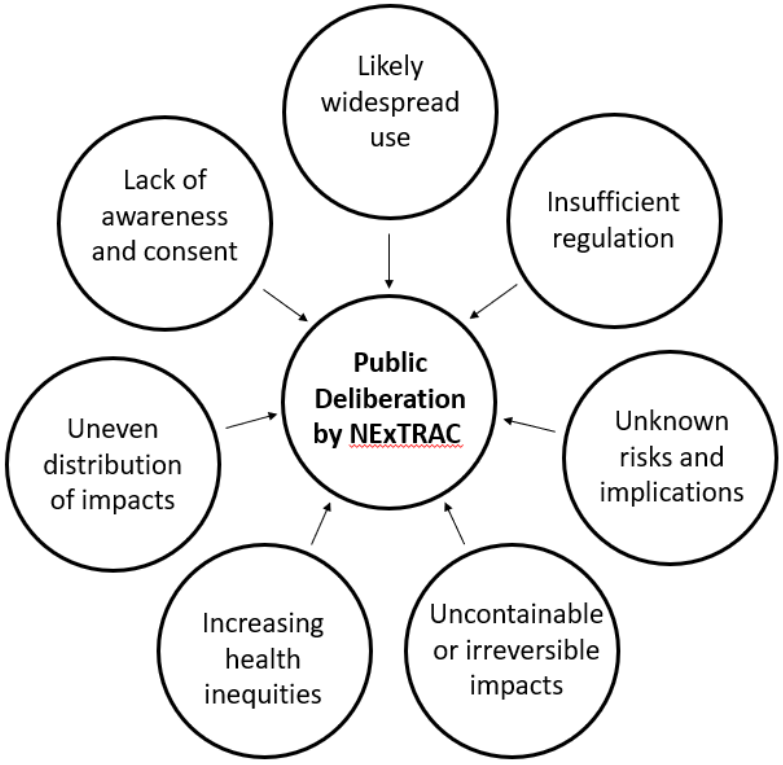
[5] Solomon, S., & Abelson, J. Why and when should we use public deliberation? *Hastings Center Report* **42(2)**, 17–20 (2012).

about which topics and tasks merit the attention of the committee, the NIH Director should consider areas and questions where public deliberation by the NExTRAC is likely to advance the discussion about considerations associated with an emerging biotechnology or application. Situations without diverse values requiring difficult balancing and specification of principles or tradeoffs where all parties agree on risks and benefits have less potential to benefit from public deliberation (e.g., if there is agreement that there is little benefit and many risks to a biotechnology or application). The working group also acknowledges that both risks and benefits are important to consider when deliberating about an emerging biotechnology or application.

Table 3. Prompts for Public Deliberation by NExTRAC

Prompts for public deliberation	Description of prompts	Examples of relevant principles or values
Likely widespread use	*The biotechnology or application could be reasonably anticipated to "emerge" into widespread use within the next decade rather than being hypothetical or at early stages of development.*	**Relevance and timeliness**
Insufficient regulation	*The biotechnology or application is anticipated to cross over into multiple scientific and regulatory domains or into inadequately regulated domains once it emerges.*	**Oversight and transparency**
Unknown risks and implications	*The ability to anticipate and mitigate risks could be limited by unique or complex scientific, safety, and/or ethical considerations associated with a novel biotechnology or application, or with expanded capabilities of an established biotechnology or application.*	**Nonmaleficence and justice** **Safety and risk management**
Uncontainable or irreversible impacts	*The ability to contain the biotechnology/application or its products, or to reverse the impacts of the technology or application on the individual or community receiving the intervention, is limited.*	**Nonmaleficence** **Safety**
Increasing health inequities	*The biotechnology or application has the potential to increase health disparities.*	**Equity and justice**
Uneven distribution of impacts	*Specific populations and individuals are expected to experience a particularly high probability or magnitude of effects from known or anticipated scientific, safety, and/or ethical risks and benefits of the emerging biotechnology or application.*	**Fairness**
Lack of awareness and consent	*Implementation of the biotechnology or application could affect individuals and/or communities who have not been informed or given consent.*	**Autonomy and respect for personhood** **Nonmaleficence**

Figure 1. Prompts for Public Deliberation by NExTRAC



1. **Likely widespread use:** *The biotechnology or application could be reasonably anticipated to "emerge" into widespread use within the next decade rather than being hypothetical or at early stages of development.*

Public deliberation may be warranted when progress in the development of a novel biotechnology or technology application indicates it is likely to advance to the point of emergence and implementation within the next 5-10 years (or sooner). This timeline is consistent with the interval to anticipated implementation and widespread use recommended by the National Academies of Sciences, Engineering, and Medicine and reported in *Preparing for Future Products of Biotechnology* (2017).[6]

Public deliberation by the NExTRAC is most likely to be productive and beneficial when the biotechnology or application is sufficiently mature to have defined features and applications.

Broad accessibility of a biotechnology or application would increase the number of individuals and communities affected by scientific, safety, or ethical considerations. As one example, the novel biotechnology or application may be (or will be in the future) available through direct-to-consumer or other broad distribution capacity.

[6] National Academies of Sciences, E., and Medicine. Preparing for Future Products of Biotechnology. (The National Academies Press, 2017).

2. **Insufficient regulation**: *The biotechnology or application is anticipated to cross over into multiple scientific and regulatory domains or into inadequately regulated domains once it emerges.*

A biotechnology or application could emerge simultaneously in several different areas and have unique applications in each area. Different scientific, engineering, and manufacturing communities may have specific regulatory processes and considerations and vary in their degree of familiarity with scientific, safety and bioethical issues. The relevant regulators may be unaccustomed to human participant protections and clinical trials, or unfamiliar with the relevant stakeholders (particularly for novel innovators). Some domains may not have effective oversight for the novel biotechnology or application. In some cases, existing strategies for assessing safety, scientific, and/or ethical risks and benefits may not be reasonably expected to effectively transfer to the novel biotechnology or application, or there may be a lack of transparency and oversight to evaluate or minimize harms and/or enable benefits. Public deliberation of biotechnologies or applications may be especially warranted in such situations. Such public deliberation would contribute to the development of more appropriate levels of oversight and more relevant guidelines for research ethics. It would also increase the transparency of NIH oversight which can earn public trust in NIH and its policy decisions.

3. **Unknown risks and implications**: *The ability to anticipate and mitigate risks could be limited by unique or complex scientific, safety, and/or ethical considerations associated with a novel biotechnology or application, or with expanded capabilities of an established biotechnology or application.*

Public deliberation may be warranted when the safety, scientific, and/or ethical issues associated with an emerging biotechnology or application have few or no comparators for risk/benefit assessment and mitigation. The biotechnology or application may also be sufficiently different from current technologies/applications such that safety, scientific, and/or ethical risks are unknown or poorly characterized and difficult to quantify. The absence of well-defined or accepted standards, and the inability to effectively conduct monitoring may also impact the need for public deliberation. This could also be true in cases where current methods and protocols to assess safety, toxicity, and efficacy might underestimate toxicity and adverse effects, and under- or overestimate efficacy. Deliberation in such cases should also incorporate discussion of the potential benefits of such technologies.

Public deliberation could be beneficial when existing technologies have evolved to the extent that they acquire significant new capabilities or applications that raise novel or unforeseeable risks or ethical considerations. Advancements in biotechnology reagents and methods, materials sciences, computational sciences, electronics, and medical devices could result in the emergence of new capabilities and applications by removing limitations and barriers to implementation and wide use. For example, implanted or injectable sensors have become increasingly networked and complex, and evolved to incorporate AI and machine learning (ML). The integration of AI and ML into existing biotechnologies and applications has the potential to raise novel ethical concerns, change the balance or nature/substance of competing values upon which decisions about the public good were based, and exacerbate existing health disparities or divisions. Each of these potential impacts are well-suited for public deliberation. Novel biotechnologies and new capabilities of existing technologies have the potential to mitigate or remove scientific, safety, and/or ethical concerns, shifting the benefit/risk assessment in such a way that public deliberation could be useful for revisiting discussion of these considerations.

4. **Uncontainable or irreversible impacts**: *The ability to contain the biotechnology/application or its products, or to reverse the impacts of the technology or application on the individual or community receiving the intervention, is limited.*

Public deliberation may be warranted in a variety of cases when there is a lower likelihood of containment and reasonable potential for off-target effects. Public discussion of the associated potential risks and benefits of biotechnologies and applications with the following features could be particularly beneficial: the products of an application are designed for uncontained or open release in the environment or for release but have a reasonable potential for spread beyond the targeted population or environment; there is potential for alteration/change in risk profile after administration or release; or there is potential that escaped or released organisms or communities will become dominant among local and regional populations. Lack of methods to safely reverse or eliminate results of administration or products of release in the event of an adverse effect may increase the value of public deliberation about a technology or application.

5. **Increasing health inequities:** *The biotechnology or application has the potential to increase health disparities.*

For the purposes of the work of this document, we define the terms equity,[7] health equity,[8] health disparities,[9] and social determinants of health[10] as described in the associated references. In short, equity refers to proportional representation (by race, class, gender, etc.) in opportunities. Health equity is the state in which everyone has the opportunity to attain full health potential and no one is disadvantaged from achieving this potential because of social position or any other socially defined circumstance. Health disparities are a particular type of health difference that are closely linked with social, economic, and/or environmental disadvantage and that adversely affect groups of people who have systematically experienced greater obstacles to health based on their racial or ethnic group; religion; socioeconomic status; gender; age; mental health; cognitive, sensory, or physical disability; sexual orientation or gender identity; geographic location; or other characteristics historically linked to discrimination or exclusion. Social determinants of health are the conditions in which people are born, grow, live, work, and age, and which are shaped by the distribution of money, power, and resources at global, national, and local levels.

Inequitable distribution of a biotechnology could affect socially disadvantaged or marginalized populations or people of color to a greater extent than other populations or individuals; and exacerbate existing health disparities. For example, a particular technology or application might benefit populations with access to or awareness of it, but increase health disparities by remaining beyond the reach of individuals who lack appropriate insurance coverage or financial

[7] Winston-Salem State University. *Strategic planning at Winston-Salem State University: Working towards equity.* (n.d.). Retrieved from https://www.wssu.edu/strategic-plan/documents/a-summary-of-equity-vs-equality.pdf.
[8] World Health Organization. *Health equity.* (n.d.). Retrieved from https://www.who.int/topics/health_equity/en/.
[9] U.S. Department of Health and Human Services. *The Secretary's Advisory Committee on National Health Promotion and Disease Prevention Objectives for 2020. Phase I report: Recommendations for the framework and format of Healthy People 2020. Section IV: Advisory Committee findings and recommendations.* (2010). Retrieved from: http://www.healthypeople.gov/sites/default/files/PhaseI_0.pdf.
[10] World Health Organizations. *Social determinants of health.* (n.d.). Retrieved from https://www.who.int/social_determinants/sdh_definition/en/.

resources required to access it, or experience barriers to access.[11] In such cases, public deliberation may be warranted to gain insight into real-world experiences as well as aspects of cultural, religious or other belief systems of disadvantaged or marginalized populations that should be considered in public policy recommendations but about which an expert panel such as the NExTRAC would be unaware. As such, public discussion could inform more viable, equitable and just policy recommendations that address what steps might be taken to promote health equity and avoid exacerbating social determinants of health.

6. **Uneven distribution of impacts:** *Specific populations and individuals are expected to experience a particularly high probability or magnitude of effects from known or anticipated scientific, safety, and/or ethical risks and benefits of the emerging biotechnology or application.*

Public deliberation may be warranted when the known or anticipated risks and benefits of a biotechnology or application are higher for a particular segment of the population or for specific individuals than for others. Cases where there could be a high probability or a high magnitude of harm or benefit to large populations and/or exponentially amplified effects could also benefit from public deliberation by the NExTRAC. In particular, deliberation may be warranted in circumstances where benefits have historically been distributed such that some populations or individuals do not receive the benefits.[12] In one example, resources for production or distribution of a biotechnology or application may be limited and make prioritization necessary. In such a case, public deliberation can lead to alleviation or reduction of exclusion and distrust by providing transparency to the policy decision process and provide a means of ascertaining public values relevant to prioritization for the collective good. In other cases, there may be a range of potential benefits, and public consideration could inform policy recommendations that ensure more of these can be realized.

Particular attention and deliberation may be needed in cases where the biotechnology or an application may disrupt the integrity or change the nature of personhood. For example, some implantable technologies have the potential for intervention in thought processes of recipients of the technology, which could undermine volition by allowing another person or a computer to act through the recipient.

7. **Lack of awareness and consent**: *Implementation of the biotechnology or application could affect individuals and/or communities who have not been informed or given consent.*

In some circumstances, there is a potential for a biotechnology or application to have an effect beyond the targeted individual who has consented, which may raise issues that would benefit from public deliberation. Public deliberation may also be warranted in cases where voluntariness and autonomy of those who are likely to be impacted by the biotechnology or application may not be fully addressed by existing practices or oversight structures. For example, continuous monitoring data collection can capture the data of individuals who have not

[11] M. Beauchemin, G.M., Hillyer, and D.G., & St Germain, D. Improving awareness and access for minority and medically underserved communities. *Clin J Oncol Nurs*, 2019 Apr 1; **23(2)**, 220-223 (2012).
[12] Regnante, J. M., Richie, N. A., Fashoyin-Aje, L., Vichnin, M., Ford, M., Roy, U. B., Turner, K., Hall, L. L., Gonzalez, E., Esnaola, N., Clark, L. T., Adams, H. C., Alese, O. B., Gogineni, K., McNeill, L., Petereit, D., Sargeant, I., Dang, J., Obasaju, C., … Chen, M. S. US cancer centers of excellence strategies for increased inclusion of racial and ethnic minorities in clinical trials. *Journal of Oncology Practice* **15(4)**, e289–e299 (2019).

given their consent, without their awareness. In such cases, public deliberation provides a transparent process for weighing the competing values of individual autonomy and the aggregate public good. Other examples include open release of gene engineered organisms such as insects carrying gene drives that have potential to spread outside of the target area, and the use of gene engineered microorganisms as probiotics that could spread to individuals and communities other than the treated individual.

B. Potential Process by Which the NExTRAC Will Consider or Evaluate any Given Emerging Biotechnology or its Applications

The working group developed the following potential process as part of the framework for NExTRAC deliberation of issues surrounding emerging biotechnologies and applications. There are a wide range of topics that the NExTRAC may be asked to consider in the future, informed by the prompts outlined above. Charges delivered by the NIH Director may be scoped narrowly or widely, and a variety of approaches may be needed in different circumstances. The working group recognizes that it is not possible to anticipate all future possible charges, or specific approaches to address those charges. Indeed, attempting to anticipate all possible emerging technologies or applications may impose unnecessary bounds on the thinking of the group.

As such, the working group developed the following process steps, which can occur iteratively and non-sequentially, where one step can inform another. The proposed process is intended to provide a flexible framework for future NExTRAC consideration or evaluation that can be applied in a charge-specific manner.

1. Assess the type of deliberation needed
2. Evaluate the scientific, safety, and ethical considerations
3. Determine how public engagement would be of benefit and identify effective methods

When the NExTRAC is given a charge by the NIH Director, they (or a working group of the committee) will likely first assess the type of deliberation that is needed. The process of deliberation may depend on number of factors, such as the charge's scope, timeline, and the level that the technology has emerged.

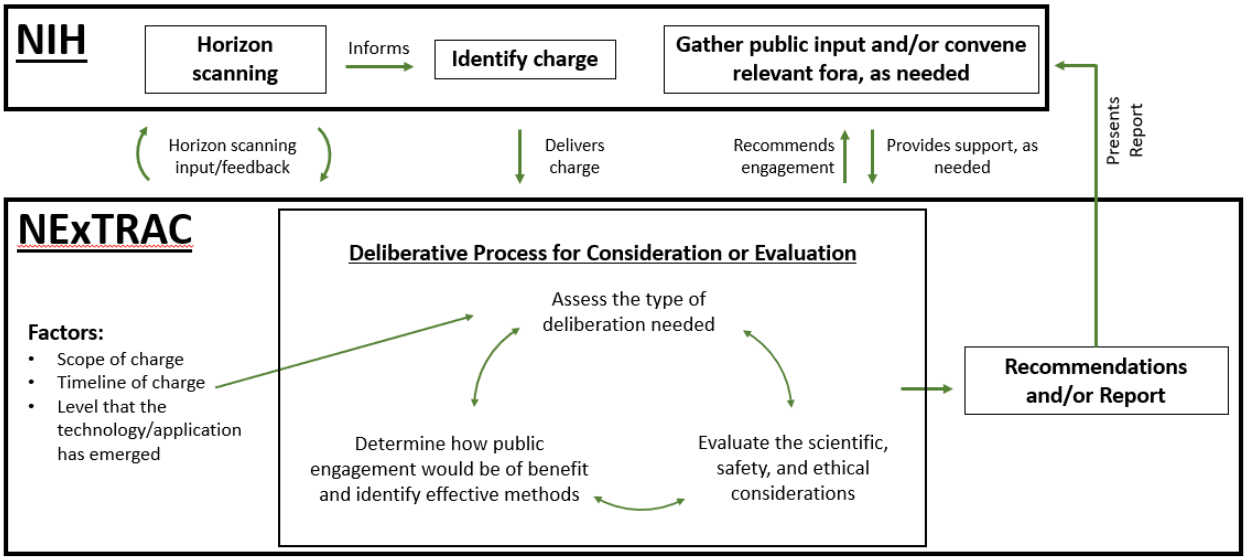
The committee/working group should also evaluate the relevant scientific, safety, and ethical considerations and how those considerations may be addressed by current or future regulation. Such evaluation can be done through desk research, and workshops and meetings with field-specific experts, etc. This assessment can also help inform how public engagement would be of benefit and identify effective methods of soliciting feedback and engaging the community.

Public engagement has value independent of the charge and, as needed, NIH can gather public input for the committee/working group to consider or NIH can convene relevant fora to allow the committee to engage directly with relevant stakeholders. This public engagement and input may take a variety of forms, including forums, workshops, requests for information, listening sessions, public broadcasting of the committee's or working group's charge, progress, and results, etc. The committee/working group should also identify a timeline and strategy for optimal public engagement on a charge-by-charge basis. Previous groups have considered these issues, and their work can be used to inform appropriate engagement strategies for

different specific charges.[13,14,15] For example, stakeholder engagement, particularly from patients, has helped identify barriers related to clinical trial enrollment and is becoming an increasingly critical component of a successful clinical trial.[16,17] There are benefits with public engagement at various points in the process. Early engagement could promote public trust and be beneficial to identifying key stakeholders, issues, and considerations, which may inform the rest of the process. In contrast, late engagement could allow for potentially more directed discussions.

The deliberations of the NExTRAC and any relevant working groups may also serve as a potential information source in horizon scanning efforts by NIH. Following this process, the NExTRAC will provide their recommendations and/or report to NIH. This process is described in Figure 2 below.

Figure 2. Potential Deliberative Process for NExTRAC Consideration or Evaluation



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