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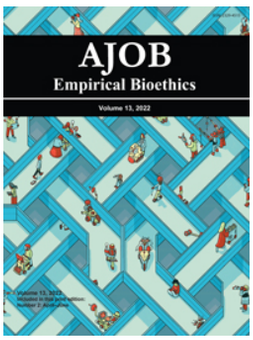

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Governing Gene Drive Technologies: A Qualitative Interview Study

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ABSTRACT

Background: Gene drive technologies (GDTs) bias the inheritance of a genetic element within a population of non-human organisms, promoting its progressive spread across this population. If successful, GDTs may be used to counter intractable problems such as vector-borne diseases. A key issue in the debate on GDTs relates to what governance is appropriate for these technologies. While governance mechanisms for GDTs are to a significant extent proposed and shaped by professional experts, the perspectives of these experts have not been explored in depth.

Methods: A total of 33 GDT experts from different professional disciplines were interviewed to identify, better understand, and juxtapose their perspectives on GDT governance. The pseudonymized transcripts were analyzed thematically.

Results: Three main themes were identified: (1) engagement of communities, stakeholders, and publics; (2) power dynamics, and (3) decision-making. There was broad consensus amongst respondents that it is important to engage communities, stakeholders, and publics. Nonetheless, respondents had diverging views on the reasons for doing so and the timing and design of engagement. Respondents also outlined complexities and challenges related to engagement. Moreover, they brought up the power dynamics that are present in GDT research. Respondents stressed the importance of preventing the recurrence of historical injustices and reflected on dilemmas regarding whether and to what extent (foreign) researchers can legitimately make demands regarding local governance. Finally, respondents had diverging views on whether decisions about GDTs should be made in the same way as decisions about other environmental interventions, and on the decision-making model that should be used to decide about GDT deployment.

Conclusions: The insights obtained in this interview study give rise to recommendations for the design and evaluation of GDT governance. Moreover, these insights point to unresolved normative questions that need to be addressed to move from general commitments to concrete obligations.

KEYWORDS

Ethics; qualitative research; gene editing; gene drives; governance

Introduction

Gene drive technologies (GDTs) bias the inheritance of a particular genetic element within a population of non-human organisms, thereby promoting its progressive spread across this population. If successfully developed and deployed, GDTs may be used to counter intractable problems. GDTs could, for example, be used to target vector-borne diseases such as malaria and to control invasive species and agricultural pests that humans thus far have been unable to resolve through other means such as bed nets, insecticides and pesticides (Gantz et al. 2015; Esvelt et al. 2014; Neve 2018). Various types of GDTs using different molecular mechanisms have been proposed, ranging from non-localized gene drives intended to spread throughout a population or species, to localized or threshold-dependent gene drives that are spatially or temporally limited in their spread (NASEM 2016; Alphey et al. 2020). In the past few years, GDTs have advanced substantially, raising the prospect of moving from laboratory experiments to environmental field studies with gene drive organisms[1] (Thizy, Coche, and de Vries 2020).

The possibility of using GDTs to alter organisms in our shared environment raises a range of ethical

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questions and issues. One key issue in the debate on GDTs is how their development and potential deployment can be guided responsibly – in other words, what governance[2] is appropriate for these technologies. As has been recognized in the literature, GDTs have a large transformative potential: they could have significant benefits as well as harms and could affect a wide range of stakeholders (Thizy et al. 2019; Nuffield Council on Bioethics 2012; Rudenko, Palmer, and Oye 2018). This raises moral questions about how the various interests should be balanced, who should be involved in decisions about the development and deployment of GDTs, and in what way. In discussions about these matters, there has been particular attention to the role that communities living near the site of field trials should play (Neuhaus 2018; Kolopack and Lavery 2017). It has also been noted that GDTs could spread across national borders, such that their governance warrants a transnational approach (Noble et al. 2018; NASEM 2016). Additionally, the development of GDTs is likely to encompass long-term transnational collaboration between researchers in high-income countries (HIC) and low- and middle-income countries (LMIC), where GDTs are most likely to be deployed given the higher incidence of vector-borne diseases (NASEM 2016).

Emerging technologies such as GDTs have several features that make procedural validity and fairness especially important for the legitimacy of governance procedures (Kuzma 2020; Kuzma et al. 2018; Nuffield Council on Bioethics 2012; IRGC 2015). First, GDTs are characterized by substantial uncertainty about the potential benefits and risks of their deployment due to the inherent complexity of ecosystems and the limitations of the extent to which laboratory conditions and mathematical models can model the real-world (De Graeff, Jongsma, and Bredenoord 2021; Marchant, Abbott, and Brown 2013; Nuffield Council on Bioethics 2012; Rudenko, Palmer, and Oye 2018). In addition, different stakeholders have ambiguous understandings of the prospects that GDTs offer and divergent moral views on whether, and if so under what conditions, to deploy GDTs (De Graeff, Jongsma, and Bredenoord 2021). Ambiguity makes it difficult to come to a shared understanding of the substantive criteria that governance decisions should be based on, and uncertainty complicates the evaluation of such criteria (Marchant, Abbott, and Brown 2013; Nuffield Council on Bioethics 2012). For these reasons, procedural criteria are all the more important (Kuzma 2020; Kuzma et al. 2018; Nuffield Council on Bioethics 2012; IRGC 2015; Neuhaus 2018).

Different policies have been proposed to govern GDTs, ranging from voluntary consensus statements to (inter)national regulation. Various policy papers and consensus statements have been published in which academics and scientific organizations have outlined recommendations and principles for GDT research and policymaking (Oye et al. 2014; Akbari et al. 2015; Adelman, Akbari, et al. 2017; Adelman, Pledger, et al. 2017; Carter and Friedman 2016; Emerson et al. 2017; James et al. 2018; Long et al. 2020; Roberts et al. 2017; NASEM 2016), ranging from safety recommendations for laboratory research (Akbari et al. 2015; Adelman, Pledger, et al. 2017) to core commitments for field trials with localized GDTs (Long et al. 2020). These manuscripts provide recommendations for different actors that play a role in GDT research and development, including researchers, policy makers and funders of GDT research. Moreover, academic associations and scientific authorities have published guidelines on GDTs and related policy-making (WHO/TDR and FNIH 2014; AU & NEPAD 2017; NASEM 2016; Sustainability Council of New Zealand 2018; Australian Academy of Science 2017; RIVM 2016). Finally, GDTs are governed by various national and transnational agreements, such as the National Environmental Policy Act (NEPA), the Convention on Biological Diversity (CBD) and its Cartagena Protocol on Biosafety (Reynolds 2020; Thizy, Coche, and de Vries 2020).

While governance mechanisms for GDTs are to a significant extent proposed and shaped by professional experts in the field, the published consensus papers and policy papers are by their nature inapt to explore the convictions of these experts and potential differences between them in more depth. It is valuable to study the perspectives of GDT experts as doing so can deepen the understanding of governance issues by providing insights into how they view and weigh different ethical aspects (Rehmann-Sutter, Porz, and Scully 2012). Moreover, it can help to identify questions and concerns that have thus far been underrepresented in the literature, and thereby broaden the scope of issues that warrant further evaluation. In this study, we therefore investigated experts' perspectives on GDT governance through a qualitative interview study. We considered it important to investigate the perspectives of GDT experts as they are likely to shape both the design of GDTs and to influence related governance frameworks[3].

Methods

The findings reported here are part of larger qualitative interview study that investigated professional experts' moral views on GDTs. Qualitative interviews

are a valuable method to identify, better understand, and juxtapose people's perspectives; in this way, qualitative research can improve the understanding of ethical implications of a technology by providing insights into how interviewees contemplate different ethical aspects (Rehmann-Sutter, Porz, and Scully 2012). This article reports on the findings related to the procedural ethical aspects of GDTs, i.e., the questions, concerns, and implications that relate to the process of governance of and decision-making about GDTs[4]. In what follows, we provide a concise summary of the study methodology, which has been described in more detail elsewhere (De Graeff, Jongsma, and Bredenoord 2021).

Participant selection and recruitment

Participants were considered eligible for study inclusion if they had contributed to academic publications and/or policy documents on GDT research and development. Eligible participants were identified through a review of the academic (de Graeff et al. 2019) and policy publications on GDTs and based on recommendations by previous participants, i.e., through snowball-sampling. The research protocol was submitted to the research ethics committee of the University Medical Center Utrecht for review before initiation of research. The committee determined that this study was exempt from the Medical Research Involving Humans Act (research proposal no. 18/618). In line with the submitted research protocol, participants were first informed about the study and agreed to participate via e-mail, and verbal informed consent for participation in the interview, recording of the interview and data analysis of pseudonymized transcripts was obtained prior to the start of the interview. Recruitment was ended when saturation was reached, i.e., when subsequent interviews no longer brought up new issues ('coding saturation') and the formulated themes were sufficiently understood ('meaning saturation') (Hennink, Kaiser, and Marconi 2017).

Data collection

Semi-structured interviews were conducted by NG. The topic list for the interviews was based on a previous review of the ethical arguments related to GDTs (de Graeff et al. 2019) and discussions amongst the research team. The interviews consisted of open-ended questions related to the potential benefits, risks, broader ethical implications, and governance of GDTs. This semi-structured design allowed participants to bring up or emphasize specific issues they considered relevant, whilst also ensuring some consistency in the topics that were discussed to explore how different participants viewed these topics. The interviews were recorded, transcribed verbatim, and pseudonymized.

Data analysis

The pseudonymized transcripts were analyzed thematically (Braun and Clarke 2006). An initial coding list was developed based on the topic list, familiarization with the data, and discussion in the research team. Subsequently, NG coded a sample of the transcripts. KRJ critically (re)read this sample of coded transcripts, and the interpretations and suitability of the codes were discussed and compared amongst the research team. The coding list was evaluated and adapted, and all interviews were coded by NG using Nvivo 12 software. A research assistant, IP (see acknowledgements), also coded 20 interviews, and the coding between NG and IP was compared. The meaning of individual text fragments was determined by interpreting them in the context of the whole interview with the participant (Kvale 1994). In the course of analysis, codes were adapted, and additional codes were added to the coding list where necessary. A meaning pattern was identified across the data set, leading to the formulation of interpretative higher order themes. Throughout the analysis process, the research team went back and forth between the different steps to allow for constant comparison. Finally, relevant quotes were selected to illustrate the identified themes.

Results

Out of the 43 experts that were approached, 33 agreed to participate in the study, 8 were unable to participate and 2 did not respond. A total of 33 semi-structured interviews were conducted between November 2018 and July 2019 with experts from

Table 1. Respondent characteristics.

Discipline	*n*
Natural sciences*	11
Ethics/philosophy	8
Non-governmental organization (NGO)	5
Policymaking	4
Social sciences	4
Country of primary employment	
United States	13
United Kingdom	11
Other European countries (BE, FR, SP, CH, NL)	8
Burkina Faso	1

*Respondents who worked in the natural sciences and affiliated with an NGO (n = 2) were classified under 'natural sciences'.

different disciplines and countries (see Table 1 for respondent characteristics). The interviews lasted between 49 and 114 minutes, with an average duration of 69 minutes.

The respondents brought forward a range of issues they considered of importance for the governance of GDTs. Broadly, these could be clustered around three main themes: (1) engagement of communities, stakeholders, and publics; (2) power dynamics, and (3) decision-making. In what follows, we discuss the different issues that were raised by the respondents in relation to these themes. The tables list representative quotes that were selected to illustrate the identified themes.

Theme 1: Engagement of communities, stakeholders, and publics

Almost all respondents agreed that it is important to engage communities, stakeholders, and publics[5] in GDT research, yet they had diverging views on the motivations for engaging these groups, what they should be engaged in, and who should be responsible for engaging them. Moreover, they outlined various complexities and challenges related to engagement. In what follows, this will be discussed in more detail. Relevant quotes are listed in Tables 2 and 3.

Reasons for engagement (Table 2)

Broadly speaking, four overarching reasons to engage communities, stakeholders and publics could be distilled from the interviews. These reasons were not mutually exclusive, and many respondents mentioned several reasons for engagement.

The first reason was that people who would be affected by GDT deployment should be involved in decisions that could (positively or negatively) affect them for reasons of justice. These respondents argued that persons who could be affected should be given the opportunity to contribute to shaping the development of GDTs and have a say in decisions about GDT deployment (Quote 1 A). At the same time, respondents had different views on when individuals or groups would be sufficiently affected to warrant their engagement. Correspondingly, respondents used this reason to argue in favor of involving different groups, including communities, (specific) stakeholders, or publics at large. Some respondents also argued that the degree to or way in which groups could be affected should determine in what way particular groups should be engaged, for instance arguing that while a broad range of stakeholders should be engaged, only potential beneficiaries should get a say in decision-making about deployment (Quote 1B). A few

Table 2. Engaging communities, stakeholders, and publics.

	Reasons for engagement	
	Summary	Illustrative quote
1A	Engagement of those affected is necessary for reasons of justice	R21: "The best thing to do is to try to give everybody a chance to have their say. Especially the people that would be most directly impacted by the release of a gene drive in an area. (..) That's really fundamental to doing this. Their environment's going to be altered, their health is (..) maybe placed at risk, so they have to have a say in the release of a gene drive into the environment. There needs to be public engagement too as far as giving everybody with a stake in the gene drive a say in the decisions that are made. That would include obviously people with environmental concerns. But also industry, religious groups, anybody in society that has some stake in gene drives."
1B	A broad range of stakeholders should be engaged, but the focus should be on potential beneficiaries	R5: "What we want to do is to engage everyone, but make sure that the center of the engagement is on beneficiaries and giving them - they can say at the end that they don't want it. (..) [they are] the ones to make decisions."
1C	A fair process could legitimate its outcome	R22: "My personal experience is that (..) people who are very skeptical of genetic engineering and think it unlikely that they will eventually support the release and vote in favor of releasing the [gene edited organisms], are still strong supporters of the project because they think that this is how technology should be developed, that you should go to the community and ask the community what they want and invite the community to guide the research and development stage. And so, they support the project even though they don't actually support the idea of genetically engineering [organisms]."
1D	Engagement could contribute to responsible development of GDTs	R32: "We need diversity of disciplines, need diversity of world views, need diversity of perspectives to really do this responsibly because there are so many blind spots that will be involved in this really complex technology interacting with ecosystems which are also highly complex, not to mention the political, geopolitical and societal situations".
1E	Engagement could prevent public backlash	R16: "In the long run, it might avoid like backlash after, I would say ten years of research and then your innovation is just considered like, no, it's not going to go outside of the lab."
1F	Engagement could inform different groups about the research	R15: "The community and the public engagement's really key and those discussions are really important (..) people need to know what they're talking about and understand what they're talking about to actually be – for it to be a meaningful discussion."
	Timing and design of engagement	
1G	Engagement should start in an early stage of the research process	R21: "I think if you're going to do community engagement, it needs to be done really early on in the process so that it's not a fait accompli. It's not like a thing that's already - a done deal. So the community really feels that they're being heard and they have a say."

respondents mentioned that a fair process in which communities, stakeholders or publics are engaged in the right way could legitimize its outcome (Quote 1C). What they considered the 'right way' differed among respondents, as is further explored in the next subsection.

The second reason was that engagement could contribute to more responsible development of GDTs or to better decision-making. Respondents pointed out that publics, but particularly communities and broader stakeholders can bring up new viewpoints, questions and concerns that can help reduce blind spots (Quote 1D). The third reason was that engagement could help to ensure that GDT deployment would be acceptable to these different groups and could prevent public backlash (Quote 1E). The fourth reason was that engagement could educate and inform these different groups about the research that is taking place (Quote 1F).

Timing and design of engagement (Table 2)

Engagement can take many shapes and forms, and respondents' views on the timing and design of engagement strategies also depended on how they motivated its importance.

Many respondents considered it essential to engage stakeholders 'upstream', i.e., early on in the research process GDTs and related governance could still be shaped by their input (Quote 1C/1G). At the same time, it often remained unclear what such engagement should consist of, and respondents had different views on this matter. This can be illustrated by the list of different issues in which communities, stakeholders and publics should be engaged according to different respondents, which included providing input on funding choices, taking part in outreach activities, having access to complaint mechanisms, participating in deliberative discussions, giving approval for each stage of the development of GDTs in stage-gate processes, and deciding about final deployment.

Other respondents focused on the 'downstream' engagement of communities and/or other stakeholders in decision-making about deployment, as such engagement could legitimate the decision to deploy GDTs. On this point, too, respondents agreed on the overall aim, yet different in their views of *how* these groups should be engaged in such decision-making (see 'Theme 3: Decision-making models').

Complexities and challenges of engagement (Table 3)

Respondents also mentioned several challenges for and complexities of engaging communities, stakeholders, and publics. First, various respondents mentioned bias or framing of the provided information on GDTs can unduly influence the engagement process. While several respondents praised the engagement efforts that the gene drive community are undertaking (Quote 2A), other respondents were critical of engagement processes led by scientists, who in their view necessarily have a conflict of interest by virtue of their role in the research (Quote 2B). Correspondingly, several respondents argued that stakeholder engagement should be controlled by an independent third party that has less personal interest in the outcome of the discussion or deliberation. Whilst respondents from the natural sciences did not mention this as a reason to abstain from playing a role in engagement processes, they did bring up their stake in GDTs being successful (Quote 2C). One respondent argued that funders should make funding available for independent parties to conduct engagement processes.

Second, respondents mentioned engagement processes can be time and resource intensive (Quote 2D). Some respondents also noted engagement of communities and publics can be a challenge due to the complexity of the science (Quote 2E), whereas a few other respondents underlined that it should not be assumed members of the public do not understand science (Quote 2F). Some respondents mentioned that public engagement tools and processes should be adjusted to specific contexts, such as literacy levels, to facilitate understanding. Moreover, a few respondents suggested that people who participate in engagement processes should be compensated for their time.

Third, a few respondents argued that some engagement processes are a farce; they contended that although everyone agrees engagement is important, the input of those engaged is hardly ever taken seriously and/or they are not given true decisional capacity because it is not an integral part of institutions and scientific practice (Quote 2G). Other respondents argued that engagement processes often only focus on the science, whereas they should focus on other aspects too (such as the underlying values, the way in which technologies should be governed, and what to fund in the first place) (Quote 2H).

Theme 2: Power dynamics

Another prominent theme in the reflections of respondents related to the power dynamics that may be present in relation to GDT research and deployment. Respondents stressed the importance of not repeating historical injustices regarding decision-making in

Table 3. Complexities and challenges of engagement.

	Complexities and challenges of engagement	
	Summary	Illustrative quote
2A	The gene drive community handles engagement well	R1: "I like how it's being handled by the field – that there is a lot of commitment, that stakeholders are actively involved."
2B	There is a conflict of interests if scientists are responsible for engaging stakeholders	R32: "[There are no] alternative ways of public engagement [that are] not only run by the technology developer itself, which I believe is an inherent conflict of interest. (..) You have an organization seeing benefits strongly and risk lower, they are providing information about the technology and they're running the public engagement. That's going to bias the decision-making."
2C	GDT scientists have a large academic interest in GDTs working	R28: "I try to separate myself from the theorist and who's proposing something to be done in the real world (..) a lot of theorists would like to see their theory tested. I'm not the person to ask because my name is on the [important gene drive] paper. (..) People talk about conflict of interest in terms of money. (..) I think academics are driven by things other than money. If an academic says: I predict that starlight will be refracted by gravity, or I predict that a gene drive can be contained by daisy-chain, I have a high motivation to test that prediction, possibly a higher motivation than: Oh, you're going to get $1-billion if the gene drive works. Academics don't need much money, most of them don't have expensive hobbies like collecting cars, they have expensive hobbies like collecting centrifuges."
2D	Engagement processes are time and resource intensive and can be too demanding	R28: "And the problem with inclusion of public isn't that scientists don't want to include the public, it's the public doesn't want to be included. It's boring. It's time consuming. They've got a day job, you know, it's very hypothetical."
2E	There needs to be a certain level of understanding for informed deliberation to take place; this can be a challenge	R33: "And frankly, informed deliberation is the key. (..) You have a difficulty because at the very local level there's a question of education, at the national level there's also the question of developing sufficient capacity for evaluation and assessment. (..). Informed consent requires an understanding of the technologies, environmental effects and health benefits and it is going to be difficult to expect a family (..) to fully understand the range of issues. (..) Developing a (..) capacity for engagement on these issues is something that's necessary, but that takes time."
2F	It should not be assumed that people do not understand science	R13: "We shouldn't presume that people are ignorant of science. Actually, people buy into science, use scientific language, medical language to assert credibility and to show that, you know, they do their own research about you know, what is the science, so we shouldn't presume that they do not know what gene drive is and we are going to fill in the gap. But it's all the stuff with public understanding of science. That's a bit of what happened with GMOs [genetically modified organisms], presuming that people don't know. (..) people do research and often become experts."
2G	Some engagement processes are a farce as these are not embedded in institutional structures	R22: "The typical person - when approached with this question of if you're developing a technology to change the shared environment, should you go and talk to the people who live there first and ask them what they think about it and which version of the possible technological options they would prefer? Is that the right thing to do? - Everyone says "yes", everyone says "it's wrong to keep it a secret and just develop something that's likely going to be forced down their throats later on", and everyone says, "It's wrong to deny people a voice in decisions intended to affect them, that they won't be able to opt out of". (..) Everyone seems to agree with this point, it's just that's not enough to make institutions change, it's not enough to change the incentives of science".
2H	Engagement should not just focus on science, but also on values	R17: "We are testing the way that society thinks about this. And during that process there is a public consultation. But publics are only allowed to talk about science. They're not allowed to talk about these other aspects [the different values that are at play in risk assessment]. And there's been a push for a long time or a recognition for a long time that that's insufficient, that we need to open that space out somehow. But there is no model for doing that and we've failed to achieve that in Europe and in North America. And now for some reason we think we can do that Africa with this gene drive mosquito."

LMIC, and recognized various dilemmas that researchers face in view of these issues. In what follows, these considerations will be explored in more detail. Relevant quotes are listed in Tables 4 and 5.

Power dynamics in partnerships between HIC and LMIC (Table 4)

Many respondents commented on the potential power imbalances that may be present if scientists from HIC develop GDTs for potential deployment in LMIC. Various respondents argued it is essential to prevent repeating the longstanding precedents of unjust decision-making in the global South by people from the global North[6] (Quote 3A), for instance during the colonial period, in the governance and decision-making about GDTs. Some respondents commented that they considered it problematic if these technologies were developed by scientists who do not live in the region where GDTs may be deployed for the first time because risks may be perceived differently when one is not subject to them oneself (Quote 3B).

Respondents also suggested various ways to mitigate these issues and concerns and stressed the duties of researchers in this regard (Quote 3C). Most importantly, various respondents said that the inclusion of local communities, scientists, or organizations in the development and/or decision-making about these technologies can help mitigate these power imbalances (Quote 3D; see also Theme 1). Similarly, some respondents argued it is important to support and strengthen the local infrastructure so that different countries could independently govern GDTs (Quote 3E). One respondent argued this is indeed what is being done in Burkina Faso, and that

Table 4. Power dynamics in partnerships between HIC and LMIC.

	Power dynamics in partnerships between HIC and LMIC	
	Summary	Illustrative quote
3A	It is essential to prevent repeating the long-standing precedents of unjust decision-making in the global South	R27: "[A risk related to deployment of GDTs could be] repeating a precedent that we've set many times in history allowing small groups controlling a powerful technology to just force it on the rest of the world. Only in this case we're doing it at a global scale much more rapidly. I would say that's an existing risk. It's unfortunately been a part of human history too often. And I'd rather set a precedent that is opposite [to that] rather than repeating my predecessor's mistakes."
3B	It is problematic if GDTs are trialed elsewhere since risks may be perceived differently if one is not subject to them oneself	R2: "I think it's strange that we're talking about a technology that may be deployed in Africa. Although it'll be discussed and deliberated there, it remains a Western technology that we'll present there. (..) we develop a technology of which we're not sure, like, is it sufficiently safe, but we think we may deploy it in an area where we don't live."
3C	Scientists should think about their intentions and how they approach foreign communities	R25: "In general and in countries with a colonial past, you obviously have to be very careful when you approach people, with all your good intentions. And of course, you should ask yourself: 'to what extent do I have a missionary zeal, and is that legitimate, and how will that come across? (..) how do you work, how do approach and deal with people, and to what extent do you really respect people as they are?"
3D	Inclusion of local communities, scientists and/or organizations can help mitigate these power imbalances	R29: "There is a strong history of global North countries making decisions that heavily impact countries and communities in the global South. Rather than perpetuating patterns of colonialism, extraction of resources which are not ours, the approaches to address public health and conservation issues need to be community driven, they need to be approaches which are supported by and are healthy for frontline communities."
3E	It is important to support local infrastructures so that countries can independently govern GDTs	R25: "I think the ideal scenario (..) and the one in which you have the best control over, let's call it, colonialist tendencies, [is] that you (..) strengthen the scientific infrastructure regionally. And that you help with, ultimately that researchers, scientists and public health authorities in the countries themselves can take control, that they can implement the technology themselves."
3F	Local scientists are involved in the development of GDTs in Burkina Faso; this is not reminiscent of colonialization.	R7: "I saw an article in a paper saying that now you know Europe or you know US now, they have a new way of colonizing Africa. (..) This is something like, okay what do you mean? There is a technique, so the technique should stay somewhere and we as Africans, we should not try that? If we say okay this is something that we're gonna try, wére gonna work on that and [people] say yeah well it´s colonization. [But] we also studied with so many people that are involved in the project and they did post-docs in the US and they had experience. So they know what they are doing. So it´s crazy [to consider it a new way of colonization]".
3G	It should be kept in check whether power is actually redistributed	R17: "There is a language being used, the language of co-development (..). this is a language which is coming from the UK in a very sort of strategic way. (..) I'm more skeptical of the real kind of sharing of power that might be going on, that there's potential for but isn't actually happening yet."

this is thus not at all reminiscent of colonial practices (Quote 3F). Another respondent, in contrast, argued that power is not actually being redistributed in local engagement practices in some countries where GDTs are currently being developed, and that it should be checked whether the language of co-development is brought into practice (Quote 3G).

Dilemmas related to power dynamics (Table 5)

Respondents also reflected on whether and to what extent (foreign) researchers can legitimately make demands regarding local decision-making procedures. On the one hand, some respondents argued that researchers should accept the local culture and norms and adopt local decision-making procedures (Quote 4A). If they demanded alternative decision-making procedures, a few respondents argued, they could rightfully be accused of colonialism (Quote 4B). Slightly deviating from this perspective, another respondent argued that although local decision-making procedures should broadly be followed, foreign researchers could justifiably set minimal thresholds, for instance to ensure a certain level of inclusion of women and minorities in decision-making.

At the same time, various respondents recognized that the obligation to respect local governance and decision-making structures could create tensions with the co-existing obligation to engage those affected. Some of these respondents expressed concern that GDT deployment could be considered in settings in which legitimate decision-making process is not guaranteed, for instance in countries with a government that does not respect its citizens' rights (Quote 4C). A few respondents mentioned that they considered some of these concerns relevant to ongoing GDT projects (Quote 4D). Respondents also commented on the implications for (decision-making about) potential GDT deployment. Specifically, several respondents argued that GDT research could be considered unethical if it was conducted in a context in which the conditions are not right for adequate protection and engagement of affected people (Quote 4E). Several other respondents argued that it would be preferable to conduct the first field trial with GDTs in a setting with low levels of poverty and existing participatory decision-making structures to mitigate concerns about exploitation (Quote 4F).

Respondents also reflected on the dilemmas these difficult tensions create. Some respondents stressed

Table 5. Dilemma's related to power dynamics.

	Dilemma's related to power dynamics	
	Summary	Illustrative quote
4A	Decision-making processes should be in line with the local culture and norms	R31: "[The design of community consent and authorization processes should] be very dependent on the local culture and the local norms. (..) If that's the way they make collective decisions then that's the way the collective decision should be made. The important thing, of course, is you try to reach out and provide information to all the different components of the community and so it shouldn't just be guys in the circle making a decision. It seems, at least at this point in time, the right thing to do is to go to the community and ask: 'How do you make these decisions, what's your way of doing it?' and then do it that way."
4B	Researchers should be careful with demanding alternative decision-making procedures	R25: "You might look at how they decide about spraying insecticides on a large scale. (..) Who decides that? Does every community member decide that? Do the village elderly decide, or does the health ministry just send a DDT spray crew? (..) While that does not justify the process, it does not make it legitimate or defensible in any absolute way (..) it is something you should take as a given. And then the question, then, is to what extent if you say "actually, everyone in the village should agree to that", where you get the legitimacy to [say that]. Because then you will of course soon be accused of colonialism. Then you do indeed arrive at a (..) potential culture clash about the ideology of decision-making."
4C	GDTs could be considered in countries in which a legitimate political process is not guaranteed	R10: "I worry about research being done in a place where people don't have rights, don't have their rights respected and in places where it would be very difficult for people to say no. (..) That might have to do with political structures that don't mean that people get respected, but another reason might be just extreme poverty and a research that doesn't take its responsibilities to communities seriously."
4D	In Mali there is no sense of being able to express criticism	R17: "So Target Malaria [a nonprofit research consortium that develops GDTs for malaria control] at the moment is working very much on the informed consent of communities, developing those relationships. That's part of what the GM mosquito release in Burkina Faso is and they'll be doing the same thing in Uganda and the same thing in Mali. (..) in Mali, there is no sense of being able to critique. There's no possible critique of gene drive (..) To be fair, I think part of that is driven by the fact that malaria is a very serious problem and the potential to eradicate malaria is really, you know, it's enviable and highly desirable by (..) I would think everybody in Mali. (..) that's a pretty agreed on target. How you get there is another matter and I think if you want free and informed consent (..) there needs to be an awareness, a free and informed decision-making process."
4E	GDT research and/or deployment would be unethical in a context in which the conditions aren't right for people to be adequately protected and involved	R25: "In the end you can get to a point (..) [at which] you reach the limit of what you consider acceptable conditions under which to carry out your projects, to do your research, with which you obviously withhold a population the probable chance of a successful control of that vector. If you say, well, this dictatorship, we're not going to carry out our project here – yes, of course that means that local people are withheld that opportunity. And if your commitment is actually to help those people, yeah, then what should you choose? (..) you really need to take a case-by-case decision based on the expected chances of success, the responses you gauge from a population, and (..) the nature of the regime. I can imagine that there are regimes you don't want to have anything to do with, and that that would be legitimate".
4F	It could be preferable to pick settings with low levels of poverty and existing participatory decision-making structures to mitigate concerns about exploitation	R33: "In some ways I actually believe that it would be kind of nice if the applications were to human health on Martha's Vineyard in Nantucket. You know why? No one can say that you're exploiting a poor population to experiment on them because Martha's Vineyard in Nantucket are the richest areas of the country. (..) you also have high educational levels, high incomes, a functioning form of government town meeting with pretty broad participation. So (..) work in those settings I think sets an example of non-exploitative engagement."
4 G	The need for research and interventions is greatest in countries with unstable political systems or vulnerable populations	R31: "We always hear these criticisms about starting in Africa because people are worried the decision-making capacity is not there. It's incumbent on those who are supporting this technology to make sure it is there. I mean, the rationale for starting in Africa is not because you can get away with murder there, the rationale is because we're trying to address and interact with a problem there."
4H	Not doing research in areas with vulnerable populations may also make them more vulnerable	R10: "You know, there are fragile states of one kind or another so it's not straight forward. I'm also weary (..) of the idea of not doing research on populations simply because they're vulnerable. I think that's potentially a way of make them more vulnerable. (..) A good example would be research with pregnant women, that kind of thing. We've spent so long kind of avoiding that, that actually in the end pregnant women don't get the kind of treatment that are designed for them so they're worse off anyway. That doesn't mean you should just go and do anything you want with pregnant women or with people in poor countries, but it does mean there are special responsibilities in those kind of contexts I think. So, it's hard."

that some countries or regions with fragile political systems are also hit the hardest by vector-borne diseases, and therefore the need to consider GDT deployment is highest in these areas (Quote 4 G). Other respondents remarked that not testing new technologies in areas with 'vulnerable' populations may in fact make these populations more vulnerable, for example because the status quo puts these populations at increased risk of disease (Quote 4H). One of these respondents stressed the importance of accountability in research settings with a fragile political structure and high levels of poverty. According to this respondent, it could be justifiable to carry out research in such settings as long as the researchers could give a good account of why a particular location was picked, why research was

conducted in a particular way, how local communities and policymakers have been involved, and how obligations to the community have been fulfilled. Finally, several respondents commented that it is important for GDT projects to invest in and support capacity building to prevent or mitigate these concerns where applicable (Quote 4 G).

Theme 3: Decision-making

A third prominent theme in the reflections of respondents related to the governance structures that should be in place to make decisions about GDTs and their deployment. In what follows, these reflections are discussed in more detail. Relevant quotes are listed in Tables 6 and 7.

Comparing decisions about GDTs to other area-wide interventions (Table 6)

A first point of difference between respondents related to whether decisions about GDTs should be made in the same way as decisions about other environmental interventions or not, which in turn depended on whether they viewed GDTs as having exceptional characteristics. Broadly, four different positions could be discerned.

First, some respondents contended decision-making about deployment of GDTs should be consistent with decision-making about other area-wide (environmental) interventions. These respondents did not consider GDTs to have unique characteristics that warrant specific governance structures. Within this group, some respondents argued that they did not see any grounds to deviate from commonplace decision-making procedures that are currently used to make decisions about other interventions that could potentially affect a wide area, such as nuclear power plants (Quote 5 A). Other respondents in this group agreed decision-making about deployment of GDTs should be consistent with decision-making about other area-wide environmental interventions, but argued that the way in which decisions are currently made about interventions in our shared environment is generally inadequate and should thus be improved for all such interventions (Quote 5B).

Second, some other respondents took an opposite stance, arguing that decisions about GDT deployment cannot be made in the same way as decisions about other environmental interventions. These respondents contended that the self-propagating character of GDTs makes them unlike other environmental interventions because of their potential negative impacts and consequences (Quote 5 C) and argued that there is no adequate governance system in place that is apt to decide about technologies with such characteristics (Quote 5 D). On these grounds, these respondents argued in favor of a moratorium on GDT deployment. Other respondents argued against a moratorium because they considered it an overly cautious approach in which the potential benefits of GDTs cannot be investigated (Quote 5E). Some others argued a moratorium is unrealistic (Quote 5 F) or would create false reassurance if it was a voluntary agreement amongst different parties (Quote 5 G).

Third, many other respondents agreed GDTs have certain unique characteristics (such as the impossibility of opting out or the level of uncertainty and risk involved with their deployment) compared to other environmental interventions, yet argued this warrants the development of novel or additional governance mechanisms rather than a moratorium. For instance, several respondents mentioned more stakeholder input on GDT decision-making is warranted than is usually the case for other area-wide interventions (see Theme 1). Moreover, some respondents argued any GDT research should undergo a regulatory check before it is executed (Quote 5H). Additionally, several respondents mentioned measures that should be implemented to increase regulatory control over GDT research, including a registry of GDT experiments (Quote 5I), more surveillance, and a whistle-blower encouragement system (Quote 5 J) to flag any suspicious research.

Fourth, some respondents argued that decision-making about GDT deployment would pose unique challenges as this could affect a very large number of countries, parties, and individuals, but argued this issue should be resolved by adapting the technology rather than the decision-making procedures. They argued in favor or developing localized or threshold-dependent GDTs that are spatially or temporally limited in their spread rather than non-localized GDTs intended to spread throughout a population or species. Several respondents argued that they considered localization a necessary condition for a first deployment of GDTs because this would, in their view, be the only way to overcome or sufficiently mitigate these decision-making challenges (Quote 5 K).

Decision-making models (Table 7)

A second point of difference between respondents related to the decision-making models that should

Table 6. Comparing decisions about GDTs to other environmental interventions.

	Comparing decisions about GDTs to other environmental interventions	
	Summary	Illustrative quote
5A	We can use the same governance mechanisms for decisions about GDT deployment as for other area-wide environmental interventions	R8: "We do manage [to make decisions about other area-wide or community interventions]. (..) We do manage to talk about fluoridic water and clean air and - not, you might say, not very effectively, but nonetheless (..). And we occasionally manage to build roads and sewer plants and once in a blue moon nuclear power stations. (..) You can try, you know, terms like direct democracy and referenda (..)..That is not how we normally do things, that is not how we decide whether to give planning permission for a new housing estate, put in a new road, a sewer, a bypass or any other multi-person infrastructure thing. That's not how we do it. We do some sort of representative democracy, so we have local representatives (..) do that stuff. What's the difference? (..) So you could just say just ask the [entity that has] authority for whatever it is. (..) If they say yes then you're done. The bar has usually been, for GM mosquito stuff and probably new technologies in general, has generally been set quite a lot higher than that."
5B	The way in which we generally decide about interventions in our shared environment is not adequate	R21: "I lived in a community (..) where routinely there was mosquito spraying. (..). There were trucks that went down the alleyways in the summertime and sprayed a bunch of pesticides. And I don't think I ever got to vote on that. It was just a mosquito control board whoever was in charge, she got to say whether this was a good thing or not. (..) I don't feel so good about [that]. I really do think I should have had more of a vote or maybe I should have at least had more awareness of the ability to (..) give input to the board."
5C	There should be a moratorium because of the potential negative and irreversible consequences of GDTs	R29: "Gene drives are designed to drive a particular trait through an entire species and could have far-reaching and unpredictable, negative impacts and consequences for organisms and the environment. This technology has raised a number of red flags regarding its potential applications in agriculture, for use in bioweapons, its potential use in conservation. (..). That's why (..) we need an international moratorium on the use of gene drives for release into the environment or into agriculture."
5D	There should be a moratorium because we need to develop a fair regulatory system	R32: "I'm not anti-technology in any way, I'm anti only certain people getting to decide how it gets used. Again, I think there needs to be maybe some more space for just reasonable reflection on what we're really dealing with and what needs to maybe be in place to safeguard it because everything is inadequate right now: the technology's not ready, the regulatory systems are not ready, the input from the public isn't ready. There's just so much that's still missing."
5E	A moratorium is an overly precautious approach	R12: "The reason I'm against the moratorium is that I think we ought to push back a little bit against this overly precautious approach. (..) I think in order to make an informed decision about whether we should be doing field trials or more general releases, we really need to know a lot more about what the technology can and can't do. And so we're kind of, to issue a moratorium now would just be making a choice in the dark. And I think that the potential benefits are far too great to make that kind of uninformed choice."
5F	A moratorium is unrealistic, so we should focus on ways of doing this as safely as possible	R33: People that say (..) 'we oppose extinction drives, we don't want to be seeing research in this area, we want to be seeing prohibitions indefinitely on release', I want to say: it's unrealistic. I cannot image India standing for that position when people are dying of malaria. And India has the technical skills to be able to do it quickly. (..) I don't want to be saying 'just because someone's going to do it, stop talking', no, but I'm saying if you hold out with too stringent a set of conditions it's going to happen. So let's get together and focus on ways of doing this as safely as possible."
5 G	A moratorium would offer false reassurance	R28: "Almost every time I bring up surveillance it's usually because a bunch of academics are posturing that all we have to do is sign a document: Let's get a lot of signatures on this document where we have a moratorium and it will be a voluntary moratorium. And, in fact, they're very thrilled that it's a voluntary moratorium, and I say: 'Come on, man! We've got an involuntary moratorium on introducing wild species because of the EPA, and on introducing pharmaceuticals because of the FDA, why do we need a voluntary one on top of that?' (..). The moratorium is (..) just like a false reassurance. What we want to do is stiffen up with things that are involuntary, that are regulated."
5H	Any GDTs should undergo a regulatory check before it is executed	R2: "The [regulatory] system in the Netherlands used to be set up in such a way that if you are allowed to do work at the lowest [safety] level, you don't have to register for it every time. So, if you already had permission to work with CRISPR-Cas and you thought, I'm going to turn that into a gene drive, [the regulatory authorities] wouldn't see that. When we realized this, it was immediately – alarm bells, we have to do something about this. Then we specified that if certain conditions are met (..) you need to apply for a permit. Then it comes to the attention of the authorities, so to speak, and then a risk assessment can be done that considers all kinds of issues."
5I	There should be an (international) registry of GDT experiments	R20: "I think one pre-condition [for GDT field trials] is that (..) there should be transparency, I think that's very important. So in human genome editing there's a lot of discussion about the need for registering for the experiments in international database, so that everyone knows what's going on. And I think there could be similar efforts in this area."
5J	A whistle blower encouragement system should be set up to flag suspicious research	R28: "In addition to surveillance we need consequences. You need a whistle-blower encouragement system: if anybody sees something, they should be encouraged to say something. How do you do that? This came up with the CRISPR babies. A lot of people who knew about the CRISPR baby project and they didn't say anything to anybody other than to the person doing the experiment: Don't do that. (..) You've got to do more than that (..)."
5K	Localization is a necessary condition for a first field trial or release	R26: "First field trials for sure need to be like a localized drive. We need to do quite a bit of testing. And you've got to do it in a controlled way so localized it is, because that way at least you don't need pan-continental agreement."

eventually be used to decide about GDT deployment, with different respondents proposing different decision-making models to achieve this.

One respondent suggested that individual informed consent to GDT deployment is warranted (Quote 6 A). In contrast, multiple other respondents noted that individual informed consent is not suitable for public health interventions such as GDTs (Quote 6B). According to some of these respondents, individual informed consent would only be required if the people

Table 7. Decision-making models.

	Decision-making models	
	Summary	Illustrative quote
6A	Individual informed consent is warranted	R29: "Applications are interesting as intellectual exercises but we really need to think about the technology platform of this extinction technology: (..) Who's making the decisions? Where are the global, international regulations and assessments? Who needs to give consent? If this is a technology designed to drive across all borders and boundaries then everyone affected needs to give their consent and that means everyone."
6B	Individual informed consent is not suitable for public health interventions	R22: "Informed consent is something that maybe appropriate for medical ethics, but it is not appropriate for public health and no one has ever suggested seriously that it is."
6C	Individual informed consent is only necessary for research participants	R31: "Individual informed consent would only be required for people who actually meet the standards of human subject research."
6D	Individual informed consent is undesirable for public health interventions	R8: "And it's also difficult, I mean, another thing that comes up in this area (..) is the deliberate confusion [by anti GM (genetic modification) activists] between this sort of area-wide technology and an individual based medical trial (..) or intervention. (..) The argument then is if somebody is going to be in the area of GM mosquito release then that's an experiment on them, which is not really true, but let's say, and you need their individual informed consent. OK? Or you can turn that around and say that means that everybody in the release area should have an individual veto on this collective action. Which (..) is incredibly anti-democratic."
6E	Consent should be obtained on a community level	R12: "We don't think that individuals just need to be informed about what's happening, they need to provide active consent to it. Now obviously that's going to be much more difficult in a public health context or in the context of a GMO [genetically modified organism] environmental trial because you can't necessarily go around knocking on everyone's door and asking if they want to have this trial or not. But I think there are certainly political procedures you can use to try and get something more closely approximating community consent."
6F	Direct democracy approaches based on majority rule are undesirable for they do not give enough space to minorities	R3: "I do not like democracy by majority rule. (..) Democracy is that all minorities get space. Not just to exist, but to express themselves and to influence policies. The majority rule is an emergency procedure. We can't figure it out, so we'll resort to voting."
6G	Direct democracy approaches are undesirable for decision-making for they are prone to be influenced by mere sentiments	R4: "I do not think it is realistic to say that we should all decide together, that it should be a democratic decision, because then you get something like Brexit. That was very important, yet people voted based on all kinds of sentiments, that may not have overseen what the consequences would be. And well, that would, you would also run that risk if you, for example, you were going to hold a referendum on this, about whether we do or do not want a gene drive."
6H	Decision-making should be based on deliberative discussions with diverse voices	R10: "You have to pay special attention to making sure that, and this is where it moves into sort of the deliberative democracy kind of space (..), you have to pay particular attention to the sorts of people who usually get excluded from those discussion. You have to pay particular attention to diversity of voices and it's really important to pay attention, deliberately seek out people who are critical and to make sure there is a proper discussion on that. So it's not to say that they should get any special kind of weight necessarily but to have a process of discussion that takes difference seriously and probably includes it."
6I	Decision-making by representatives would be best	R8: "Most people, most of the time aren't going to take the time to look at those arguments and figure out what is what. And possibly don't have the general science, whatever, background to do that. And so most people will trust other people to do it for them. (..) so, you know, the sort of trusted intermediate thing, which might be national academies or regulatory bodies or whoever it is, you know, the government (..). This is actually how most things work."

involved could be considered research participants (Quote 6C). Moreover, respondents pointed out that it would be unjust to apply individual informed consent to public health interventions such as GDTs because it would allow individuals to trump the needs of the collective (Quote 6D). Finally, various respondents remarked that it would be practically impossible.

For these reasons, almost all respondents were in favor of obtaining consent on a community level (Quote 6E), yet they differed in their views on how such a community consent process should be shaped. Several respondents commented that they considered direct democracy approaches[7] based upon a majority rule problematic because this would not allow minorities to have sufficient influence on decision-making (Quote 6F) or because such approaches are prone to be influenced by mere sentiments (Quote 6G) such as an uninformed fear of the unknown. To counter this, various respondents were in favor of using deliberative democracy approaches, in which a final decision would be preceded by deliberation, as this would facilitate more in-depth reflection on different arguments and would allow more diverse viewpoints to be taken into account (Quote 6H).

A few other respondents argued that indirect decision-making by representatives would be best because people would not have the background and time to make an informed decision about such a complex issue (Quote 6I). Finally, several respondents stressed it should not be either/or; there should both be agreement by or consensus of the relevant transnational organization(s) (such as the African Union, the New Partnership for Africa's Development (NEPAD),

and/or the World Health Organization (WHO)) as well as some form of community agreement or consent.

Discussion

To our knowledge, this is the first in-depth qualitative study focused on professional experts' perspectives on GDT governance. Three main themes were identified, relating to (1) engagement of communities, stakeholders, and publics; (2) power dynamics, and (3) decision-making. In what follows, we relate our findings to the broader literature, and highlight issues that have thus far been underrepresented or underexplored.

The challenge of moving from general moral principles to concrete obligations

In line with the GDT literature (NASEM 2016; Adelman, Akbari, et al. 2017; Carter and Friedman 2016; Long et al. 2020; Santos 2020; Emerson et al. 2017), there was broad agreement amongst respondents on the importance of engaging communities, stakeholders, and publics. At the same time, the interviewed experts had divergent views on what this should consist of. To some extent, these different views may not be incompatible: different contexts and stages of technology development may warrant the engagement of different stakeholders, in different ways and for different reasons (Degeling, Carter, and Rychetnik 2015; Abelson et al. 2003; Santos 2020; World Health Organization 2020; Neuhaus 2018). However, the broad variety of views also points to underlying, unresolved normative questions with regards to their specification and operationalization.

As philosopher Stephen Toulmin already outlined in his reflections on the Belmont Report's principles for biomedical research ethics (Toulmin 1982), it can be surprisingly easy to settle on general moral principles, but much harder to reach consensus on how these should be operationalized. The real challenge, then, lies in specifying these general commitments to concrete moral obligations that stipulate which actions should be conducted or avoided and where, when, why, how, by what means, to whom, and by whom (Richardson 1990). This challenge has also been recognized in relation to engagement in the GDT literature (Kuzma et al. 2018; NASEM 2016; Thizy et al. 2019; Thizy, Coche, and de Vries 2020; Carter and Friedman 2016; Neuhaus 2018; Hartley et al. 2021). Correspondingly, various authors have argued that an authorized organization should develop official engagement guidelines for GDTs that field studies could be audited against (Thizy et al. 2019; Thizy, Coche, and de Vries 2020; Carter and Friedman 2016). The results of this study underline the importance of such calls, and point to specific issues that should be addressed in such guidelines and in project proposals of research consortia working on GDTs more generally. Several of these issues are discussed in more detail in what follows.

Ways forward: open questions and concrete recommendations

A first question that should be explored in more depth includes when someone could be 'affected' by GDT deployment in a way that demands their engagement – in other words: when are individuals sufficiently 'affected' and when do they have sufficient 'stake' or interests to be considered communities or stakeholders that should be engaged? (NASEM 2016) It has been argued that a broad conception of interests, that extends beyond human health and safety and includes the way in which people conceptualize their relationship to nature, should be adopted to assess who could be affected by field trials and should be engaged (Neuhaus 2018). It remains underexplored, however, what these interests should consist of, to what rights and obligations they give rise, and how this should feed into governance. This question is all the more important given that GDTs are designed to spread, which means that non-localized drives in particular could affect a large number of individuals and groups (Santos 2020).

A second issue relates to how the challenges of such engagement should be approached. An important challenge noted by respondents in this study as well as in the broader literature on engagement is the tension between its demandingness – for instance in terms of its time- and resource-intensiveness for both researchers and participating stakeholders, and in terms of overcoming power dynamics – and its inclusivity (Jongsma and Friesen 2019). The risk exists that a tradeoff is made in which engagement is either tokenistic as a result of its demandingness or unfair as a result of its lack of inclusivity. Notably, this tension may be largest in contexts where engagement would be of greatest benefit, for instance in cases where those that could be impacted by the research lack power to influence it or when the distance between their expertise or values and those of the researchers is greatest (Jongsma and Friesen 2019), as could be the case in the context of GDT research. This underlines the necessity of stipulating what engagement aims to achieve, so that engagement strategies can be tailored to achieve those goals in a

meaningful and inclusive way. Another challenge is the conflict of interest that researchers may have if they are the ones in charge of designing and conducting engagement. The gene drive community deserves praise for their efforts to go beyond what regulation requires of them in terms of engagement, yet development of an independent, detailed guideline for engagement could avoid the semblance of a conflict of interest.

A third issue that should be addressed are the power dynamics that are involved in GDT research. Power dynamics may be present in any research context, yet warrant particular attention given the fact that GDTs are most likely to be deployed in countries where large social and economic inequalities exist between the different stakeholders involved and where historical injustices may still affect the way in which knowledge is produced and foreign 'aid' is perceived (Rudenko, Palmer, and Oye 2018; CSS, ENSSER & VDW 2019; NASEM 2016; Kofler and Taitingfong 2020). As the global health, co-production and community engagement literature underline (Pratt and de Vries 2018; Pratt and Hyder 2017; Walker and Martinez-Vargas 2020; Turnhout et al. 2020; Ledingham and Hartley 2021), such inequalities and histories can contribute to power disparities that could threaten the proposed ideals of co-development and 'fair partnership' between GDT developers, communities and regulators (Long et al. 2020). Real-world guidance on how to achieve true engagement and partnership in the context of these and other power dynamics is key to prevent these commitments from remaining tokenistic. Concrete ways to counterbalance power dynamics in research collaborations include explicit acknowledgement of past and present inequalities, setting research agendas in collaboration, clarifying roles and responsibilities, sharing of property rights and resources, and fair representation in authorship (Kofler and Taitingfong 2020; Gautier, Sieleunou, and Kalolo 2018; Matenga et al. 2019; Thizy et al. 2019; Turnhout et al. 2020). In interactions with communities and other stakeholders, power dynamics may moreover be mitigated by appointing independent moderators in deliberations and engagement activities, conducting research to tailor educational material and engagement strategies to diverse groups, allowing sufficient time for deliberations, and giving communities and/or other stakeholders formal power (Neuhaus 2018).

A final issue that should be explored in more depth, and that has thus far been underrepresented in the GDT literature, relates to the demands that foreign researchers may justifiably make on the way in which decisions about GDT deployment should be taken. What demands would constitute a safeguarding of important research ethics standards and rights, and when would such demands turn into cultural imperialism? While potential tensions between devising minimal criteria for responsible GDT governance and respecting local customs, social and political circumstances, and decision-making procedures may exist, several concrete recommendations can be made besides conducting GDT trials in HIC (Kuzma et al. 2018). First, this tension could be reduced by ensuring that local rather than foreign experts are in the lead in knowledge production and decision-making. The literature on GDT, and this paper is no exception – both in terms of its author list and in terms of the respondents interviewed – is mostly dominated by authors from HIC, which reflects the current reality that development of GDTs primarily occurs in these countries (Long et al. 2020; Hartley et al. 2021). This underlines the importance of evaluating who participates in the development and conduct of research on GDTs and on what basis of equality (Walker and Martinez-Vargas 2020; Hartley et al. 2021; Finda et al. 2020). Second, when it comes to specific governance mechanisms and decision-making models, this tension may provide reason to predominantly focus efforts on explicating the *goals* that such mechanisms and models should achieve, rather than the specific shape they should take.

GDTs as governance anomalies?

The results of this study also point toward the need to evaluate the way in which decisions about the development and deployment of GDTs relate to broader discussions about the adequacy of governance systems for emerging biotechnologies. As has also been shown by Sam Weiss Evans and Megan Palmer, stances on whether GDTs should be considered anomalies in governance systems are closely tied to stances on whether these broader systems are adequate or inadequate in the first place (Evans and Palmer 2018).

Next to stressing the relevance of broader reflections on whether biotechnology governance is suitable and for whom (Evans and Palmer 2018), these different stances also invite more in-depth reflection on what it is (if anything) that makes the development and deployment of emerging biotechnologies categorically different from other interventions that may affect (the world around) us, and/or GDTs different from other biotechnologies and area-wide interventions. Emerging biotechnologies more generally may for instance be seen as requiring (more) engagement

of communities, stakeholders and publics than other environmental interventions due to their inherent uncertainty and ambiguity, the remoteness of bodies such as research councils from traditional channels of democratic accountability and/or the long timescales between the development of a technology and the realization of its impact (Nuffield Council on Bioethics 2012). Compared to other emerging biotechnologies, for which a concern can be that they *might* spread, a distinguishing feature of GDTs could be that they are *designed* to spread. The most important question, in turn, is what governance measures are warranted in view of such differences. Only by pinpointing and critically reflecting upon these differences can specific governance modifications be proposed to deal with these unique characteristics. This is both important for procedural validity and fairness, and to deal with the earlier described challenge of demandingness in a broader context of research on emerging biotechnologies. As one of the respondents phrased it: "You can't have a deliberative democracy every time you do a research project" (R10).

Limitations and recommendations for further research

As reported in another manuscript based on the same study (De Graeff, Jongsma, and Bredenoord 2021), there are several limitations that should be taken into consideration when interpreting its results. First, our study was the first large and in-depth interview study on professional experts' perspectives regarding GDT governance. Correspondingly, it had an exploratory character to allow experts to bring up issues they considered relevant. Although saturation was reached on the identified codes and themes, further research should explore these topics more extensively. Second, any qualitative research is subject to interviewer and researcher bias; a different interviewer could have focused on other aspects during the interview, and another research team could have grouped the codes and themes differently. Third, our study represents a group of GDT experts that had prominently contributed to the academic and/or policy debates on GDTs. While these experts offered a diverse range of perspectives, they were predominantly employed in the global North, as was discussed previously. Subsequent research should center on the perspectives of experts in other countries, especially those in which GDTs may be deployed, who possess unique expertise on the local context of potential field trial locations that is essential for robust and legitimate governance. This is particularly important with regards to the topic of power dynamics – a theme that was not envisioned in advance, and for which more extensive reflection by experts from countries where GDTs might be deployed is indispensable. Similarly, it would be very relevant to conduct a qualitative study amongst the communities living in areas where GDTs may be deployed who possess experiential expertise that is highly relevant to GDT governance. Finally, many of the issues identified in this study warrant a more detailed normative analysis.

Conclusion

GDTs elicit diverging moral views on whether and how they should be deployed. This ambiguity and the uncertainty related to GDTs make it particularly difficult to make governance choices based on the potential outcomes of their deployment, underlining the importance of procedural fairness in governance mechanisms. This article provides a contribution to responsible guidance of GDT development and deployment by investigating professional experts' perspectives on GDT governance. The obtained insights give rise to specific recommendations with regards to engagement, mitigating power dynamics and evaluating decision-making models, and point to unresolved normative questions that should be addressed to move from general commitments to concrete obligations.

List of abbreviations

CRISPR/Cas9	Clustered Regularly Interspaced Palindromic Repeats/CRISPR-associated protein 9
GDTs	Gene drive technologies
GM	Genetic modification
GMO	Genetically modified organism
HIC	High-income country
LMIC	Low- and middle-income countries
NGO	Non-governmental organization

Notes

1. Organisms whose genomes have been genetically altered with a gene drive to spread a desired gene alteration through a population. GDTs could only be used in organisms that have an inheritance pattern that can be biased, which typically means that they reproduce sexually (Alphey et al. 2020).
2. Technology governance may be defined as the "process of exercising political, economic and administrative authority in the development, diffusion and operation of technology in societies" (Organization for Economic Co-operation and Development (OECD)) 2021). Governance thus encompasses a broad range

of mechanisms to steer technology development, including but not limited to regulation (Rudenko, Palmer, and Oye 2018; Organization for Economic Co-operation and Development (OECD)) 2021).

3. At the same time, it should be noted that the expertise relevant to GDT governance is not limited to professional expertise on GDTs, but importantly also includes what has been called the 'experiential expertise' (Harris et al. 2016) of community members living near potential GDT trial sites. Indeed, professional experts on GDTs may be laypersons on other topics of relevance to GDT governance (Nowotny 2003), such as expertise of the local environment and social-cultural context and having personal knowledge of the illness or problem that the release of GDT organisms would address (Teem et al. 2019; Bartumeus et al. 2019).
4. The findings related to the substantive ethical questions, concerns, and implications of GDTs – i.e. those questions, concerns, and implications that relate to "what is right in terms of duties, rights, and values (..) independent of any decision-making procedure" (Sollie 2009) (155) have been reported elsewhere (De Graeff, Jongsma, and Bredenoord 2021). A detailed description of the methodology of the study, in line with the consolidated criteria for reporting qualitative studies (COREQ), has also been provided in that publication.
5. The terms 'communities', 'stakeholders', and 'public(s)' were defined and used in different ways by the respondents of this study, frequently without explication of or differentiation between these categories. Generally speaking, respondents used the terms 'communities' and 'stakeholders' roughly in line with the way in which these terms were defined in a foundational report on GDTs written by the National Academies of Sciences, Engineering and Medicine (NASEM). According to this report, communities are "group[s] of people who live near enough to a potential field trial or release site that they have tangible and immediate interest in the gene drive project" (NASEM 2016, 180), and stakeholders are "person[s] with a professional or personal interests sufficient to justify engagement" (including communities) (NASEM 2016, 185). Correspondingly, we use these terms in this way in this manuscript. The term 'publics' was used in at least two significantly different ways by respondents. One the one hand, some respondents used this term to refer to what others called communities. On the other hand, other respondents used this term in line with the NASEM definition: "groups who lack the direct connection to a project that stakeholders and communities have but nonetheless have interests, concerns, hopes, fears, and values that can contribute to democratic decision making." (NASEM 2016, 184). Where the term is used in the text of this manuscript, we use the term pubic(s) in the second sense.
6. It should be acknowledged that concepts used to divide the world also oversimplify it (Schneider 2017). Where we use the terms 'global North' and 'global South', one may also read 'Minority World' and 'Majority World' – terms that do more justice to the fact that the largest share of the world population is located in the global South.
7. I.e. approaches in which people would have a direct say in whether GDTs are deployed or not, for instance through voting.

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Conflicts of interest

Annelien Bredenoord is a member of the Dutch Senate. She also serves as a member of the Ethics Committee of the ISSCR and the Ethics Advisory Board of IQVIA. Nienke de Graeff, Karin Jongsma and Jeantine Lunshof have no conflicts of interest to declare in relation to this research.

Ethics approval

Participants were informed about the study and agreed to participate via e-mail. Prior to the start of the interview, participants were verbally informed about the interview study, its recording and the pseudonimized analysis of interview data. Each participant gave verbal consent to the interview, which was recorded. The research protocol was submitted to the research ethics committee of the University Medical Center Utrecht for review prior to the initiation of research. The research ethics committee determined that this study was exempt from the Medical Research Involving Humans Act (research proposal no. 18/618).

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Appendix 1– interview guide

As specified in the Methods 'Data collection' subsection, the interviews consisted of open-ended questions related to the potential benefits, risks, broader ethical implications, and governance of GDTs. The semi-structured design of the study ensured consistency in a number of topics to be discussed by all participants, while also allowing participants to bring up or emphasize particular new issues they considered relevant. This article reports the interview findings related to what may be classified as the procedural ethical questions, concerns, and implications of GDTs. We have reported on the findings related to the substantive ethical aspects of GDTs in a separate manuscript (De Graeff, Jongsma, and Bredenoord 2021).

1. Can you introduce yourself and explain in what way you are involved with or have experience with gene drive technologies?
2. How do you view gene drive technologies based on your experience?
    a. Potential benefits, risks, hazards, ethical implications?
    b. How should we deal with these?
3. How do you view the different potential applications of gene drive technologies (eradicating vector diseases, controlling invasive species, controlling agricultural pests)?
4. How do gene drive technologies relate to alternative strategies to achieve these goals, in your opinion?
5. Various types of gene drives, as well as various gene drive designs are under development. Do you know these different gene drives, and if so, how do you view these?
6. What are, in your opinion, conditions under which gene drive technologies could be used, or limits that should be in place?
7. Who should make decisions about the development and possible use of gene drive technologies? What should, for example, be the role of scientists, the government or governments, and citizens?
8. Do you have experience with current regulation or safety standards for research with (and development of) gene drive technologies? If so, what do you think of the current regulation and safety standards/what should be addressed in such regulations or standards?
    a. Should this be approached in an international context? If so, how?
9. How should gene drive research develop, as far as you are concerned?
    a. For example, what would be needed to draw conclusions about whether or not gene drive technologies should be applied and if so, how?
10. Are there topics that have not been addressed that you would still like to discuss?