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Procedural legitimacy: co-developing a community agreement model for genetic approaches research to malaria control in Africa

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Abstract

With reductions in the malaria burden stalling in the past years, gene drive holds promise as a novel way of reducing disease transmission. Governance and decision-making processes are pivotal aspects of the legitimate adoption of this technology. Here, the authors explore Target Malaria's journey in developing a community agreement model for the release of non-gene drive genetically modified mosquitoes. They describe the iterative development of the model, including consultations with experts, stakeholder engagement, and alignment with principles of procedural justice. Several challenges were identified during its development, including defining communities, ensuring adequate information, consultation, monitoring, and achieving a common decision between dissenting and consenting viewpoints. They underscore the complexity of developing a legitimate model and emphasize the importance of transparency, procedural legitimacy, and adherence to ethical principles. This paper does not describe the model itself, which will be the subject of another paper. Instead it focuses on the process, to share this experience with other projects—those working with gene drive, or any other projects requiring a community-level decision-making process. The model builds on Target Malaria's experience with the release of genetically modified sterile male mosquitoes, to address the challenges posed by modified mosquitoes which are fertile and would therefore be expected to persist longer in the environment and spread further than the sterile male mosquito strains. While the level of spread and persistence of these non gene drive, but fertile, modified mosquitoes are expected to be substantially lower than those of the gene drive mosquitoes, the process is an essential advance in accommodating the broader geographical and temporal concerns associated with the more permanent spread of gene drive mosquitoes. The work described here constitutes part of the evolution of a community agreement process that could be applied to proposals for releases of gene drive mosquitoes for malaria control. In describing this process, Target Malaria hopes to contribute to the ongoing dialogue on good practices for community agreement engagement in research for genetic vector control approaches and to share the experience of building legitimacy while designing such agreement models.

Keywords Community agreement, Gene drive, Genetically modified mosquitoes, Malaria, Field evaluation, Stakeholder engagement, Community authorization, Consent, Vector control, Co-development, Procedural legitimacy, Procedural justice, Stakeholder legitimacy, Community representation, Area-wide

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Background

After years of progress towards global malaria elimination goals, the last years have revealed the extent of the challenges ahead in achieving the goal of elimination [1]. Insecticide resistance [2, 3], drug resistance [4], the impacts of armed conflicts [5], residual transmission [6] and climate change [7] are threatening the progress made in the last decade. The reduction of malaria cases and deaths stalled for a while and is now on the rise compared to pre-pandemic numbers [1]. There is a growing consensus that new tools are required to address those challenges in a holistic way [8]. Gene drive mosquitoes are considered as one of those potential transformative complementary tools [9]. This method harnesses a naturally occurring phenomenon [10] that increases a gene's prevalence in the population through sexual reproduction. This method could contribute to malaria elimination, either by driving a gene that affects mosquito reproduction and thus reducing the malaria-transmitting mosquito population [11] or by driving a gene that affects and interrupts the parasite transmission [12].

As this technology continues to develop and research shifts from the discovery phase to potential evaluation and future use as a tool against malaria, questions about governance and decision-making are raised [13–17]. Other malaria interventions also raise governance issues but those tend to focus on accessibility, country ownership and financing. When community engagement is mentioned, it is more in the context of ensuring coverage and individual adherence than questioning whether communities are part of the broader decision on developing and using new tools [18]. When envisaging genetic approaches and, in particular, fertile strains, questions related to governance include an important focus on the role of communities—defined as "groups of people who live within the geographical location or biologically relevant proximity (e.g., flight distance of a targeted insect vector) to a potential site where research is taking place or where field releases may take place such that they have tangible and immediate interests in the research project" [19].

The legal decision-making process from authorities is well established. Biosafety laws regulate the release of genetically modified mosquitoes. In most countries, these laws are framed as the application of the Cartagena Protocol on Biosafety [20]. In the framework of the Convention on Biological Diversity, regulatory authorities are encouraged to "consult the public in the decision-making process regarding living modified organisms" (Article 23), and in the case of the release of organisms containing engineered gene drive, specific provisions were made to seek or obtain the consent from affected indigenous people when appropriate [21]. However, existing regulatory frameworks focus on obligations at the national and governmental levels and not at the community level. Policymakers and academics have established that individual consent is not the appropriate mechanism for agreement to the release of area-wide vector control tools, including those using genetic approaches [22–25]. Instead, the existing guidance on research ethics for vector control and for testing genetically modified mosquitoes proposes using "community authorization" [26, 27]. These guidance documents propose principles for this community-based decision-making process. However, due to the large spectrum of projects and contexts considered, they do not provide a specific model or approach for research and development projects to follow. Instead, the WHO advises researchers to accommodate cultural considerations that may be context-specific for any given research project when considering the need for community authorization [27]. In the absence of normative requirements for this community authorization process, research projects may develop their own models, integrating the existing principles and guidance and adapting them to their specific circumstances. The legitimacy of these models is critical for their success and ethical relevance and must be considered early, starting from the design phase of the model. The process of building legitimacy for these models is not specific to a particular technology and can be a learning opportunity for a broader set of researchers and practitioners.

Target Malaria is one of the leading projects developing gene drive mosquitoes for malaria elimination in sub-Saharan Africa [28]. The project progresses in phases, according to existing best practices and guidelines [23, 27, 29]. All three pillars of the project (science, stakeholder engagement and regulatory affairs) evolve along those phases, starting with non-gene drive genetically modified sterile mosquitoes [30] followed by the ongoing second phase of non-gene drive genetically modified male bias mosquitoes [31]. The ultimate phase will be self-sustaining gene drive genetically modified mosquitoes [32, 33].

The project uses the intermediary phases (sterile male and male bias) to develop its community agreement models. The intermediary phases also enable communities, stakeholders and national authorities in the countries concerned to be involved in informing the next steps of the research. The agreement models follow the same stepwise approach, integrating learnings from the previous phase and evolving to adapt to the next context of each phase.

This paper will describe the process followed by Target Malaria to develop its agreement model for the intermediary phase, how it built on the first model used for entomological collections and for the non-gene drive sterile

male release in Burkina Faso, and how this intends to inform future models for community agreement for the field evaluation of gene drive mosquitoes. This paper focuses on how the model has been designed and does not describe the model itself, which will be the subject of another publication. By doing so, the authors intend to focus on the process by which a model is designed and the thinking going into building its legitimacy throughout the process.

This paper focuses on the community agreement model and does not explore the approaches for individual consent that might be required for specific activities. Individual consent is sought and obtained for activities where an individual—or a household—is participating or directly impacted by an activity. For instance, as part of mosquito collections, specific methodologies require entering someone's house to collect mosquitoes using traps, aspiration, or insecticide spray catch [34]. This is the case whether they are part of the routine entomological studies to understand the existing mosquito population or part of the research protocol related to releasing a genetically modified mosquito strain. In those cases, individual consent is sought and obtained from the individual who owns or uses the specific room. The methodology to do so is standard and includes thorough information sharing about the proposed activities, associated benefits and risks, and the right for the person to refuse without any consequences on their ability to benefit from the project in the future [35]. The individual consent methodology is described in the research protocol and reviewed by the institutional ethics committee, which often monitors the implementation of this protocol [36].

Initially, the project intended to develop a model appropriate for gene drive releases and evaluate it with its non gene drive fertile strain. However, the process revealed that specific details—e.g. about the future gene drive mosquitoes field release protocol design, the conditions in which the evaluation might take place (in particular the nature of the potential partnerships in the implementing country), or the ongoing regional policy processes (in particular to deal with transboundary issues)—would need to be available before the development of a comprehensive agreement model for gene drive mosquitoes. Therefore, it was decided to focus on this intermediary phase as a stepping stone for a potential gene drive phase, as this phase encompassed the complexities of an agreement model for a fertile strain of mosquitoes, with a greater level of spread and persistence in the environment that its sterile counterparts from previous releases.

This paper explores the diversity of skills and perspectives required to develop such a model and the need to ground the model in the African research context. It also describes the various steps followed in this process (Fig. 1). By sharing the approach taken by the project to respond to these challenges, the paper intends to inform other researchers and foster discussions between practitioners, policymakers and academics about good practices to build legitimate community agreement models for genetic approaches to vector control, and more broadly for area-wide interventions. This paper focuses on the community agreement process and does not discuss the regulatory permits that are required prior to any release of genetically modified mosquitoes, which often include some public consultation process as per the Cartagena Protocol on Biosafety, Article 23 [20]. The paper focuses on the process of designing a community agreement model and does not describe the details of this model, which will be the subject of a different paper, as the authors strongly believe that the process can be an example applied to a variety of projects aiming to develop their own model for community-level decision-making, while the model itself is very specific to Target Malaria, its activities, values, and context.

Target Malaria's iterative process to develop a community agreement model for genetic approaches

The foundation of Target Malaria's stakeholder engagement strategy is the ability to integrate stakeholders' inputs, respond to local circumstances, and adapt to research findings. Flexibility and adaptation have been critical components of the project's approach to stakeholder engagement, schematized in Fig. 2 [36]. This characteristic is also critical when envisaging community agreement models. It allows the integration of emerging guidance, recommendations, and other changing circumstances and feedback (Fig. 2). The process of developing this agreement model reflects the same principle.

The existing model for field entomological collection activities and non-gene drive sterile male mosquitoes

The project initially developed its community consultation and agreement process in the context of its field entomological collections and for the activities related to the non gene drive genetically modified sterile male. This process was used for both importation and work in contained use in Burkina Faso and Mali [37, 38] and for the small-scale release in Burkina Faso of the non gene drive sterile male mosquitoes [39]. This step allowed the project to design and test an agreement model aligning with communities' preferences and context which reflected existing guidelines [36, 40].

This initial model, reviewed and approved by research ethics committees, relies on an in-depth understanding of community dynamics and governance and on

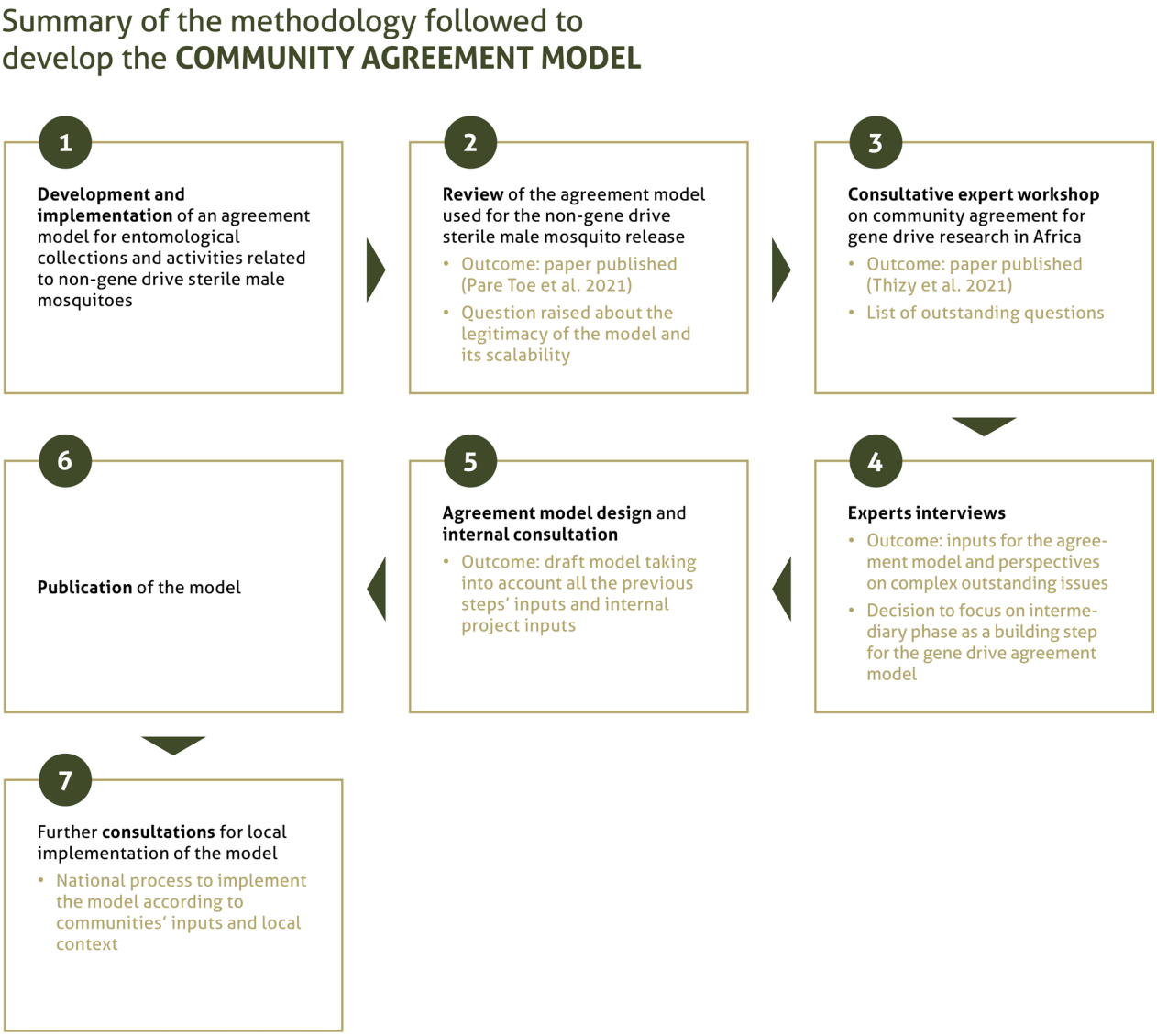

Fig. 1 Process of the methodology for developing the community agreement model

communities' inputs to co-develop an agreement model that is acceptable and legitimate for them. In the villages where this was implemented, this took the form of a group of community representatives chosen by the community and "cross-checked [by the researchers] with all village components, including minorities and vulnerable groups". It also includes several accountability mechanisms during the process, including during and after the mosquito release [36, 40]. This model builds on trust between the communities and the researchers developed over extensive engagements over a long period of time. In the village in Burkina Faso, where the non-gene drive sterile male mosquito release took place, the project had started its engagement more than 5 years prior to the release.

Review of the agreement model used for the non-gene drive sterile male mosquito release

Openness and accountability are critical not just to the model itself but to the process by which it is developed. On this basis, in 2020, Target Malaria decided to review its agreement model. This review balanced the positive feedback from the affected community and stakeholders directly involved in the process with the learnings from external observers who questioned the model and the legitimacy of the group deciding on behalf of

Fig. 2 Target Malaria stakeholder engagement strategy [36]

the community [40]. There were also concerns raised by the project itself about the ability to apply the same model to future releases of other strains. These may not afford the same lengthy period of preparation time to build trust and relationships with communities in the same way as was done for the sterile male and would likely require a scaling up of the number of field sites. The time and personnel intensity of the model would be difficult to sustain in the future. Finding the right balance between extensive in-person engagement that marks early phases and scaled-up strategies required when targeting a larger area or using a fertile strain was recognized as a key challenge. Experience from other projects working on area-wide vector control, such as the World Mosquito Program, showed that the agreement model had to evolve to accommodate different timelines and a growing number of field sites [41]. The early model allows for building understanding and trust and leaves space for co-development. In contrast, the latter allows for reaching out to more communities and more flexibility to adapt to potential changes. Gaining this scale and flexibility while maintaining understanding, trust, and co-development was at the heart of the challenge faced by the project for its next phase.

Consultative expert workshop on community agreement process for gene drive research

While the project was faced with these questions of scalability of an agreement model for the next phases, the discussions about genetic approaches to vector control and gene drive had reached a broader audience of engagement practitioners, social scientists working on global health, entomologists, global health experts and bioethicists. Proposals were made for the governance of gene drive mosquitoes without inputs from engagement practitioners or concerned communities [42]. A process was needed to involve a broad range of experts to establish the basis of what an agreement model for gene drive could be. The Pan African Mosquito Control Association (PAMCA) had organized trainings on gene drive and hosted discussions on this topic at its annual conference, and the Kenyan Medical Research Institute (KEMRI) had initiated research on the engagement practices for genetic approaches to vector control. These two organizations were natural partners to co-lead a consultation on a community agreement model for gene drive research in Africa and to anchor this process in the cultural and political context where this technology could be evaluated [43].

The workshop, co-organized with KEMRI and PAMCA, gathered experts from thirty different organizations and research institutions from Europe, North America, Asia and Africa, as demonstrated in Fig. 3 (some experts had more than one affiliation). This technology is intended for evaluation and use in Africa, so priority was given to experts from the continent. This workshop also intended to gather input from a variety of disciplines, recognising that the model should be informed by social sciences and ethics but also by engagement practitioners, entomologists and global health experts (Fig. 3). The authors used the differentiation made by the experts themselves between epidemiologists, malaria experts and global health experts. The first category refers to experts studying specific interventions and their impacts on malaria, while the global health experts focus on a broader set of issues beyond one disease and take a more interdisciplinary approach.

The consultation aimed "to provide direction and recommendations to Target Malaria, and beyond the project offer some reflections for other projects, specifically on the question of community acceptance and consent for possible future field evaluations of gene drive-modified mosquitoes". The experience with the initial agreement model and the feedback received after the release of the non gene drive genetically modified sterile male mosquitoes in Burkina Faso informed the selection of three thematic clusters for discussions: (i) representation and legitimacy, (ii) accountability and (iii) operational considerations.

The key findings from the workshop included appropriate terminology ("community agreement" vs community "acceptance" or "consent"), identification of the relevant stakeholders and community with which to engage (a distinction between relevant communities vs general public), reflections for engagement with stakeholders who may not wish for the research to take place and considering their opposing views, inability of individuals to opt-out and need for dynamic engagement with multiple decision points, and the need for monitoring mechanisms. The workshop also differentiated the degree of engagement and agreement-seeking requirements depending on how the release would impact the communities. Potential impacts could come from the activities associated with the releases (e.g. monitoring activities, media interest in the release), or from the mere presence of the research team in their village, or from the mosquito's presence [43].

Interviews with experts

The workshop identified several complex topics requiring additional reflection that were categorized into five key themes: 1. Defining communities, 2. Information and verification of understanding, 3. Consultation and community agreement, 4. Monitoring the implementation of the agreement, 5. Dissenting voices and minority perspectives.

Target Malaria's engagement practitioners developed a list of precise questions for each theme, aiming to break large concepts into practical questions that the model would need to respond to. A sample of these questions can be seen in Fig. 4.

Following the workshop, experts were interviewed to address those questions. The experts were selected

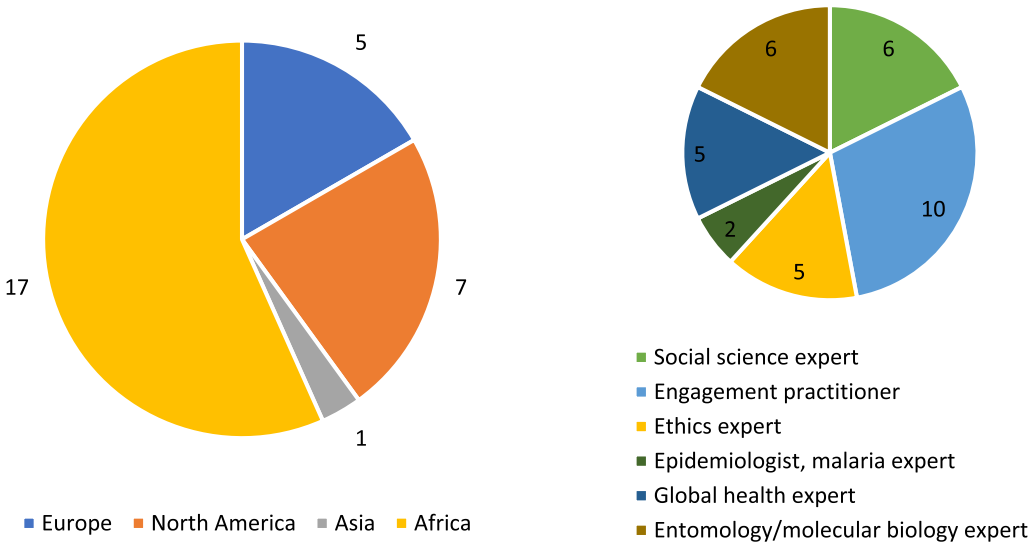

Fig. 3 Geographical representation and main area of expertise of workshop participants (according to their institutional affiliation)

Gap questions – Defining communities

- If the consent is "community-based", how is a community-defined?E.g.,is it the same as a village? Can a community be a sub-set of a village (meaning we could have several communities within a village) or be composed of several villages?
  - Where is the "border" and how is it defined? By whom? Is that "border" following administrative limits?
- Who defines what a community is?
  - Who defines who should be engaged within the community? On what basis?
  - Who qualifies as a resident of a community?
  - Do migrants qualify as residents? Do temporary residents (e.g., seasonal workers, fishermen) qualify?
- Does anyone need to confirm/approve how the target population gets defined?
  - If so, who?
  - If so, when? (e.g.,is it just before the consent process, is it early in the research process)
- For those who are in the area of influence (i.e., the area in which the released mosquitoes would reach) but notdirectly impacted bytheentomologyactivities, are thereother obligations towards them in relation to the agreement model?
- What are the ethical obligation towards the population that is not directly impacted? General public?
- How do we define that a population is directly affected by an impact on their natural resources or their use of this resource (e.g., if someone is not directly living where the impact takes place but depends on this resource – economically, culturally, socially – and that this resource will be impacted by the proposed activity)?

Fig. 4 Sample questions on defining communities for the Target Malaria agreement model used during the second consultations

according to their experience, knowledge of the specific questions, and authority on the topic, considering their participation in discussions about governance and engagement for genetic approaches and gene drive. Twenty-nine experts were consulted (some had already participated in the first workshop). This group was geographically diverse, with a higher representation of bioethicists (about 30%) and the presence of several indigenous people ("indigenous people" refers to people covered by ILO Convention 169 and the UN Declaration on the Human Rights of Indigenous Peoples [44, 45]). Experts from other sectors not consulted in the first workshop (from environmental conservation, humanitarian and development NGOs) were added to ensure a comprehensive assessment. The integration of these new disciplines and perspectives intended to reflect the growing interest and debates that were taking place about gene drive research and community decision-making process in biodiversity conservation forums (whether at the Convention on Biological Diversity meetings or in the International Union for the Conservation of Nature) and the concerns expressed by delegates from Indigenous Peoples' organizations.

Agreement model design and internal consultation

The various experts' perspectives were considered to elaborate a draft model. The clear conclusion from all the consultations was that the model could not be focused on a specific set of responses but rather a set of questions the engagement teams should ask the communities and themselves when operationalizing it. For instance, it was impossible to provide a pre-determined definition of communities, but it was possible to establish the need to work with members of a community and stakeholders in a given setting to define this community. As a result of this consultation, the project decided that part of the model would include a set of questions in the form of a checklist that would be used in the consultation with community members and stakeholders to develop the operationalized model for each territory.

Once the agreement model was drafted, all the project's functions were consulted on the proposed model and commitments to ensure a project-wide alignment and support on the proposed approach and their possible consequences on future milestones and timelines. This consultation included perspectives from regulatory, risk, entomology, contained laboratory, molecular biology, modelling, communication, and project management experts from all the Project partners (Project partners are the different research institutions that form Target Malaria [28]).

Publication of the model

The publication of the process to elaborate the model and separately of the model itself, is part of the overall process of building a legitimate agreement model for the release of genetic approaches to malaria control. The peer review process and the availability of the model for scholars, practitioners, civil society groups, stakeholders, and potentially community members are another step of the ongoing consultation about the engagement model.

Further consultations for the model's local implementation

After this updated agreement model is designed for the intermediary phase of non gene drive fertile mosquito release for research, the operational model will need to be adapted to each local context, considering the concerned communities' inputs. The model provides a framework within which community engagement teams can adapt according to cultural values and socio-political dynamics. A project-wide community agreement model aims to ensure that all communities affected by Target Malaria work on fertile strains of non-gene drive genetically modified mosquitoes follow the same guiding principles, even if the specific operationalization of this model may differ. Based on this agreement model, the project consultation with the in-country stakeholders has started in countries of operation to implement the model in the specific socio-cultural and political context.

A community agreement model development process rooted in values

Inclusiveness

The community agreement model development was based on an inclusive and open dialogue between project teams, partners and external stakeholders, particularly those from Africa and those with experience in stakeholder engagement as a social science and its practice.

The absence of explicit norms about what constitutes a legitimate, ethical, and adequate community-based decision-making process for area-wide vector control tools renders the task of developing agreement models challenging, as researchers need to identify what could be rightful and acceptable as they go. When Target Malaria designed its original model used for entomological collections and the non-gene drive genetically modified sterile male phase, the team based itself on the existing literature [22] and existing practices of similar projects [46, 47], as well as on internally available expertise. The adaptation of this model to the local context was based on the co-development approach of the project [36]. The institutional ethics review committee of IRSS' Comité d'Éthique Institutionnel pour la Recherche en Sciences de la Santé (Institutional Ethics Committee for Research on Health Sciences) which hosts Target Malaria's work in Burkina Faso reviewed the original model. Before and during its implementation, the model was also widely shared with local and national stakeholders, who provided further feedback. The consultative approach was intrinsic to the model's development, aligning with the project's values and principles [48].

The composition of the workshop and the experts list for the second consultation is intended to be inclusive in terms of geographical representation and the field of expertise and knowledge represented (for details on this composition, refer to Consultative expert workshop and Interviews with experts sections).

Building trust and accountability

The recommendation which emerged from the experts' interviews was for the project to clearly define its position on community agreement and be explicit about its commitments, ambitions and aims for stakeholders to be aware of from an early stage. Additionally, the experts highlighted the concepts of "procedural justice" [49, 50] and "procedural legitimacy" [51] as fundamental elements that inform whether a community agreement model is considered fair, ethical and responsible. In this context, the process of developing a community agreement model is considered as important as the community agreement model itself. This advice led the project to decide to publish a description of its process and the future publication of the model.

In line with these recommendations, the model establishes a clear reference framework, with commitments, key questions, and a set of values, that would be communicated publicly to a large audience and that could be used to assess how the community agreement model is operationalized in each context against a set of criteria and questions. The publication of those commitments and this reference framework will also intend to provide visibility to communities partnering with the project and hold Target Malaria accountable. It is also expected that this framework could be a valuable tool for monitoring and evaluation. Being explicit from an early stage allows the project and its stakeholders to establish a reference framework to monitor and evaluate how the agreement model is implemented, and decisions are obtained from the community. This openness and accompanying accountability are some of the conditions to build trust and are a critical element to a community agreement model which is aligned with existing guidance, but which is not defined or imposed by regulations.

Differentiating the community agreement model from the broader engagement model

The decision-making phase, resulting from the consultation, is only a small part of the engagement spectrum [52, 53]. It is often the most visible to external stakeholders as it directly impacts the implementation of activities. There is a different level of ethical responsibility towards those who should be engaged for information, feedback gathering and consultation and those from whom a form of authorization (or agreement) should be obtained before an activity (such as a release) takes place. The basis for this difference relates to the fundamental ethical principle of respect for persons and the requirement to "protect the interest of those who will be affected by the research" [27]. Appropriate engagement is increasingly considered an ethical requirement for global health projects, as it is a condition of communities' empowerment, informed participation and decision.

This agreement model is aligned with NASEM definitions [23], as the primary focus is on those potentially impacted directly by project activities i.e. the communities. The WHO Guidance framework for testing genetically modified mosquitoes states that "efforts should be made to ensure that communities, stakeholders and publics are appropriately engaged and that host communities for [genetically modified mosquitoes] release are given the opportunity to provide legitimate authorisation for the releases" [27].

While the community is the focus of the model, stakeholders and the public not directly affected by the project's activities are engaged continuously through information sharing, consultation and other methods to ensure that their knowledge and perspectives are considered in the project activities and that their concerns are addressed [36]. Inclusiveness of those other groups is a fundamental principle of Target Malaria's engagement approach [48]. The publication of this paper will contribute to informing stakeholders and the public about this model. Conferences and media are opportunities to collect feedback from global stakeholders and the public. The in-country phase of the process will also have specific activities to inform and collect feedback from stakeholders and the public in countries where the potential releases would take place. This engagement also opens the possibility for those individuals and groups to hold the project accountable to its proposed approach and thus contributes to the model's procedural legitimacy.

Looking ahead: developing a model for gene drive mosquito field releases

The project progresses in phases, with gene drive mosquitoes being the last phase. There are other projects that are developing area-wide approaches to vector control that offer similarities with the intermediary phase and learning opportunities. For example, Oxitec's sterile mosquito approach [54] is similar in terms of spread and persistence to Target Malaria sterile male mosquitoes and even to some extent to the non-gene drive genetically modified male bias mosquitoes. Similarly, the experience of the World Mosquito Program with *Wolbachia* [55, 56] offers relevant considerations for carrying engagement for area-wide vector control with a technology that spreads and persists over time, even though the *Wolbachia* mosquitoes are not regulated as a genetically modified organism. However, there are important differences between these projects and Target Malaria in terms of key considerations for a possible field evaluation. The questions related to *Wolbachia* projects' agreement model are mostly about scalability and not so much about the spread and persistence of the mosquitoes and potential transboundary issues [41, 56, 57].

Table 1 summarizes the various area-wide technologies for vector control and some of their respective complexities when designing a community agreement model.

While a lot can be learned from these other examples and their experience [41, 58], significant differences exist between those projects, the technology used, and the considerations related to a possible field evaluation of gene drive mosquitoes for malaria control (see Table 1).

The Oxitec technology used for dengue control (for example, in Brazil or, more recently, in the United States) is a self-limiting technology, requiring repeated releases to maintain efficacy, and with only minimal dispersal potential of the released mosquitoes [59], given the limited range of *Aedes aegypti* [60]. Similarly, while the replacement *Wolbachia* approach is self-sustaining, the spread of these bacteria in *Aedes* mosquitoes is relatively slow and dependent on the density of the population [61, 62].

By contrast, based on mathematical modelling, the spread and dispersal of gene drive in *Anopheles* mosquitoes is designed for and expected to be far more rapid and extensive. These features make such gene drive approaches desirable from the point-of-view of malaria vector control; they would be expected to have a sustained and long-lasting impact on mosquito populations

Table 1 Comparison of the main area-wide vector control technologies [41, 47, 65–68]

Strain/ technology	Mosquito species	Objective	Fertility	Persistence of the modification in the environment	Spread of the modification in the environment	Precedent for the technology prior to its release release into the environment	Specific complexities for community agreement model (beside complexity of explaining the technology)	Existing community agreement model	Regulatory approvals/ authorisations
Oxitec Friendly mosquito technology	*Aedes aegypti*	Suppression of dengue-transmitting mosquitoes	Fertile males, no female progeny	Self-limiting strain, the gene can be passed to the offspring but its frequency declines over time	Limited due to self-limiting characteristics and *Aedes aegypti* limited geographical spread	No release of GM insects for public health purpose before	Scalability in very large urban environments	Community engagement but no documentation of community authorisation, in the US referendum were used	National regulatory approvals under GMO/ environmental legislations required for research and wide scale use (commercial or philanthropic)
World Mosquito Program *Wolbachia* mosquitoes	*Aedes aegypti*	Reduction of the ability of mosquitoes to transmit dengue	Fertile	Self-sustaining, the Wolbachia bacteria is transmitted to the offspring	Incremental but slow due to *Aedes aegypti* limited geographical spread	No release of *Wolbachia*-carrying insects for public health purpose before	Scalability in very large urban environments	Yes, a common model with difference in implementation according to the national context	National regulatory permits as required in the legislation of the country
SIT mosquitoes	*Anopheles gambiae*	Suppression of malaria transmitting mosquitoes	Sterile	None due to the sterility	None due to the sterility	SIT in agriculture but not in public health	None	Community engagement but no documentation of community authorization	National regulatory permits as required in the legislation of the country
Target Malaria non gene drive sterile male mosquitoes	*Anopheles gambiae*	Suppression of malaria transmitting mosquitoes	Sterile	None due to the sterility	None due to the sterility	No release of gene edited mosquitoes before SIT technologies provided some precedent	None	Yes model for community agreement	National regulatory approvals under GMO/ environmental legislations required for research
Target Malaria non gene drive fertile strain	*Anopheles gambiae*	Suppression of malaria transmitting mosquitoes	Fertile	Self-limiting strain, the gene can be passed to the offspring but its frequency declines over time	Limited due to the self-limiting nature of the strain	The release of the Target Malaria non gene drive sterile male, and Oxitec friendly mosquito provide some precedent	Complexity of agreement over various geographies where the release activities might take place	Subject of this paper and of the upcoming paper describing the model	National regulatory approvals under GMO/ environmental legislations required for research

Table 1 (continued)

Strain/ technology	Mosquito species	Objective	Fertility	Persistence of the modification in the environment	Spread of the modification in the environment	Precedent for the technology prior to its release release into the environment	Specific complexities for community agreement model (beside complexity of explaining the technology)	Existing community agreement model	Regulatory approvals/ authorisations
Target Malaria gene drive strain	*Anopheles gambiae*	Suppression of malaria transmitting mosquitoes	Fertile	Self-sustaining, the gene would be passed at a high proportion of the progeny (potentially over 95%)	Incremental, the spread increases at each generation as the gene drive becomes more frequent in the population	No release of gene drive mosquitoes, the previous Target Malaria strains will offer some precedent as well as the *Wolbachia* one, though the difference in spread and behaviour between *Aedes* and *Anopheles* reduces the comparison	Complexity of agreement over various geographies and transboundary implications. Complexity of the agreement considering the persistence in time	Not yet	National regulatory approvals under GMO/ environmental legislations required for research and wide scale use (philanthropic)

across vast rural areas of Africa without the need for constant and repeated releases [63]. However, these same properties of rapid and far-reaching spread also increase the likelihood of transboundary movement. While not relevant to other vector control approaches, these considerations are important in future approaches to community engagement and community agreement [14, 64]. Specific information on the spread and persistence of gene drive mosquitoes in the environment, and the possible transboundary implications of such releases have yet to be determined empirically in field releases. However, the transboundary dimension will be a crucial issue to consider when developing the next iteration of the community engagement model. Some of the questions this raises include what is expected regarding information, consultation, and agreement of different communities, in particular outside of the country of release, as well as the roles and responsibilities of researchers and national authorities and potentially the role of regional bodies. Other considerations will also impact the development of the next iteration of the agreement model, including considerations of the scalability of agreement models to match the possibly increasing scale of field evaluations.

Some of these discussions could already be initiated at the regional level to envisage the ethical requirements for engagement and agreement-seeking in such circumstances as they could be relevant to multiple projects on gene drive for vector control. Guidance-setting and policy institutions such as the World Health Organization (and its regional offices), the African Union (and its Development Agency AUDA-NEPAD) and regional economic cooperation bodies (such as ECOWAS or the EAC) have an important role to play in driving these conversations about community engagement and involvement of affected communities in decision-making and convene countries to these discussions early on, similarly to what they are doing in the field of regulatory aspects.

The evolution of regulatory and policy conversations at the regional level will also be a key determinant for any future agreement model for gene drive releases, as these will hopefully establish the responsibilities and duties of researchers, public health actors, and other stakeholders in the eventuality of a release.

Conclusion

Existing guidelines and best practices provide helpful guidance for developers to consider when developing community agreement models. However, there are gaps in the guidance applicable to area-wide vector control, as guidance documents tend to remain general. They do not define the "community" to be consulted, mechanisms to elicit a decision, acceptable levels of agreement and dissent within a community, or any indicators to evaluate and measure whether the proposed models are ethical and legitimate to affected communities and decision-makers. As a result, developers committed to an ethical and responsible approach to community agreement must be proactive and begin to fill these gaps while prioritising a solid foundation of procedural legitimacy. Target Malaria's model design process attempts to reflect this proactive, early-stage process to guide its teams in their future strategic and operational planning.

As the project continues to advance through its development pathways towards a potential release of gene-drive mosquitoes for research, teams are anticipated to continue consulting experts and stakeholders within their countries and regions to gain deeper insights and understandings for the development of operational community agreement models.

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Author contributions

Naima Sykes and Delphine Thizy took an active role in both rounds of consultation, led the conception and the analysis for this model and of the drafting of this article Isabelle Coche contributed to the conception and the analysis of this model, designed and facilitated the first consultative workshop and provided comments to this article Lea Pare Toe participated in the first consultative workshop, contributed to the conception and the analysis of this model, and provided comments to this article. Mouhamed Drabo, Divine Dzokoto and Jude Bigirwenkya participated in the second consultation, contributed to the conception and the analysis of this model, and provided comments to this article. Alexandre Quach and Samantha O'Loughlin provided inputs into the model and comments to this article.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

As this paper does not disclose any individual information from participants, specific consent for publication was not sought.

Competing interests
All the authors are part of or consultants to Target Malaria.

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