Global **Malaria** Programme

Vector control interventions designed for malaria transmission control in complex emergencies and in response to natural disasters

PREFERRED PRODUCT CHARACTERISTICS

World Health Organization

OVERVIEW

The *Global technical strategy for malaria 2016–2030* (GTS) aims to harness and expand research to accelerate progress towards the elimination of malaria and to counteract the emerging threat of drug and insecticide resistance. It encourages innovation and the development of new tools and strategies to maintain progress in malaria control and advance towards elimination. To accelerate implementation of the GTS, in 2018, the World Health Organization's (WHO) Global Malaria Programme (GMP) reviewed its policy-making process to ensure that it is transparent, consistent, efficient and predictable. One of the outcomes of this review was the adoption of "preferred product characteristics" (PPCs) as a key tool to incentivize and guide the development of urgently needed health products. The use of PPCs is aligned with an organization-wide effort to improve communication about identified public health needs and to facilitate innovation to meet those needs.

WHO PPCs aim to:

- communicate unmet public health needs;
- stimulate development of relevant new products to meet those needs; and
- facilitate timely, effective assessment of new products, and the formulation of policy recommendations and prequalification listings.

Within GMP, the Vector Control & Insecticide Resistance Unit is developing a series of PPCs to encourage further innovation in vector control. Some of the vector control interventions deployed in complex emergencies and in response to natural disasters – namely insecticide-treated nets (ITNs) and indoor residual spraying (IRS) – have already met identified public health needs in more stable settings; other tools such as insecticide-treated tarpaulins have been specifically designed for this use case. Given the diverse mix of existing and potential new interventions and the considerable gaps in the associated evidence base, there is a need for WHO to clearly articulate the unmet public health needs for tools designed to control malaria transmission in complex emergencies and in response to natural disasters. The need for WHO to articulate this unmet public health need was identified during the ongoing revision of the *Interagency field handbook on malaria control in humanitarian emergencies (1).*

TERMINOLOGY

Preferred product characteristics (PPCs) are designed to communicate unmet public health needs identified by WHO, stimulate innovation and investment in the identified areas, and communicate the desired performance and operational characteristics of health products to address those needs. The target audience consists of product developers, regulatory agencies, procurement agencies, and funders of research and development. PPCs accommodate a number of target product profiles (TPPs).

Target product profiles (TPPs) are planning tools used by manufacturers to guide product development. TPPs generally provide much more detailed information than PPCs, such as intended use, target populations, and safety and efficacy-related characteristics. They include both minimally acceptable and preferred performance characteristics. The minimum performance characteristics should be considered a "go/no-go" decision point in the product development process. The preferred performance characteristics should reflect the ideal characteristics required to rapidly and effectively achieve a global health impact.

PREFERRED PRODUCT CHARACTERISTICS: VECTOR CONTROL INTERVENTIONS DESIGNED FOR MALARIA TRANSMISSION CONTROL IN COMPLEX EMERGENCIES AND IN RESPONSE TO NATURAL DISASTERS

Background and purpose statement

Complex emergencies are situations in which the community or society is disrupted to the point of human suffering and material loss, and the population's own resources are insufficient. Such situations are caused by a complex set of social, political and/or economic drivers, for example, when populations are displaced due to war and other conflict. Natural disasters are the result of phenomena such as earthquakes, volcanic activity, tsunamis, flooding, etc. Both complex emergencies and disaster situations have a number of factors in common that increase the affected population's vulnerability to malaria and other vector-borne diseases, as well as to infection with other diseases. Displaced communities are usually characterized by deteriorated living conditions, often with overcrowding in damaged dwellings, temporary shelters, or sharing with host families. Sanitation and water supplies may be impaired or inadequate, which often creates breeding sites for the aquatic larvae of mosquitoes and other insects. Whatever the cause, the result is a complete breakdown of the infrastructure on which the population previously relied, leading to poor access to food and effective health care.

When complex emergencies or natural disasters occur in tropical and sub-tropical areas, malaria is often a significant contributor to the consequent mortality. The two vector control interventions deployed at large scale in stable settings, namely the distribution of ITNs and IRS, are also recommended as malaria control interventions in complex emergency settings; however, these interventions may be difficult to implement due to the lack of infrastructure, high population density, and, in many cases, the absence of fixed structures to be treated with residual insecticides or to enable hanging of nets. Alternatives to these interventions are therefore required to ensure that at-risk populations in complex emergency and natural disaster settings are optimally protected.

To date, WHO recommendations on vector control interventions for these settings have been limited to tools that are widely used in more stable settings. However, it is recognized that different preferred characteristics may be needed for tools deployed in complex emergency or natural disaster settings, for example, because of the lack of fixed structures or the high density of individuals sharing the available shelters. This PPC was developed to indicate that WHO has identified vector control interventions for malaria control in complex emergency and disaster settings as an unmet public health need, and to outline the preferred characteristics of such interventions. It is anticipated that product developers will draw on this information to develop a range of TPPs for interventions suitable for these complex, dynamic and volatile situations. This PPC will be a dynamic document that will be updated as new data indicate the need to make changes to the associated parameters and characteristics and/or to the identified public health need itself.

Parameter	Preferred product characteristic
Indication	
	• Uses any mechanism expected to reduce vectorial capacity so as to provide community protection to affected populations. • Prevention of biting on the individual using the intervention is seen as an added advantage. • Reduces or prevents infection and/or disease caused by malaria in humans. • Suitable for use by/in all age groups, including women of child-bearing age, pregnant and lactating women, and children under 5 years of age.
Target population – human	
	• Populations affected at any stage of complex emergencies / natural disasters in all geographical areas at risk of malaria. In many settings these are displaced populations that move frequently as a result of the evolving emergency context, that live in temporary shelters and that are therefore at increased risk of outdoor biting mosquitoes.
Target population – disease vector	
	• *Anopheles* mosquitoes, including strains resistant to insecticides in current use (pyrethroids, organophosphates, carbamates, neonicotinoids and organochlorines). Resistance mechanisms to be overcome include: target-site (Kdr, AChE, RDL) and metabolic (monooxygenases, esterases, glutathione S-transferases). The current priority is the development of interventions effective at controlling pyrethroid-resistant mosquito populations. • Other arthropod vectors and the diseases they transmit and/or nuisance biting arthropods are considered an added advantage.
Epidemiological efficacy	
Efficacy	• Protective efficacy to reduce or prevent malaria infection and/or disease in humans in areas of insecticide, particularly pyrethroid, resistance. The level of efficacy in terms of personal and/or community-level protection should preferably be equivalent to or greater than what has been demonstrated by pyrethroid-treated nets in areas of pyrethroid susceptibility when compared to no intervention *(2)* or to the community-level protection provided by indoor residual spraying (*3*). **Note:** Due to the difficulties associated with the collection of epidemiological data in complex humanitarian emergency settings, data collected in more stable settings may make an important contribution when assessing efficacy. To generate data in emergency settings, study designs may need to be adapted to this context. The use of adapted designs should be discussed with the WHO Vector Control Advisory Group to ensure that the data generated are of sufficient quality to inform the development of WHO policy recommendations.

Parameter	Preferred product characteristic
Epidemiological efficacy (continued)	
Combined efficacy	• If the intervention is designed for use in combination with other tools, technologies or approaches, evidence of a statistically significant additive impact needs to be made available. This evidence needs to be generated using similar assessments and entomological and epidemiological endpoints as those used for already established interventions. **Note:** Due to the difficulties associated with the collection of epidemiological data in complex humanitarian emergency settings, data collected in more stable settings using populations with similar characteristics (e.g., mobile populations) may make an important contribution when assessing efficacy. To generate data in emergency settings, study designs may need to be adapted to this context. The use of adapted designs should be discussed with the WHO Vector Control Advisory Group to ensure that the data generated are of sufficient quality to inform the development of WHO policy recommendations.
Entomological efficacy	
Knockdown/mortality	• Treatment(s) with no or low excito-repellency and/or slower killing than pyrethroids should demonstrate high kill and/or sterilization of insecticide-resistant mosquito vector(s). For interventions designed to kill mosquitoes, the killing effect is required to take place within the extrinsic incubation period of the malaria parasite (i.e., < 10–14 days). • Rapid knockdown of *Anopheles* mosquitoes would be preferable in order to provide personal protection from being bitten.
Sterilization/fecundity reduction	• For interventions deploying an insecticide that reduces the fecundity of mosquitoes, it is thought that a high level (>90%) of sterilization of the host-seeking mosquito and/or a significant reduction in egg laying/hatching or larval development by the treatment(s) is required. **Note:** Until epidemiological efficacy data supporting the public health value of interventions that reduce the fecundity of mosquitoes are available and the associated entomological efficacy evaluations have been assessed by WHO, we are unable to propose specific performance standards for fecundity-reducing interventions.
Mode(s) of action	
	• Preferably acts on one or more target sites that differ from each other and, preferably, from that of pyrethroids. **Note:** WHO will utilize the classification used by the Insecticide Resistance Action Committee (IRAC) specifically designed to clarify different modes of action (https://irac-online.org/modes-of-action/).

Parameter	Preferred product characteristic
Access and affordability	
	• The intervention needs to be affordable so that it does not constitute a barrier to access, including in low- to middle-income countries. • The cost-effectiveness of the intervention should be similar to or better than that of the current standard of vector control in a specific setting.
Feasibility	
Procurement	• Should be suitable for procurement through global donor mechanisms and/or agencies providing humanitarian aid.
Distribution/Application	• Should be suitable for distribution through emergency relief channels, i.e., primarily through top-down delivery channels managed by agencies providing humanitarian assistance.
Supervision	• Little to no training requirement for deployment and use would be preferable. • Specialized tools should not be needed to deploy or use the intervention.
Regulatory	
Safety – human health	• The end use product should not pose an unacceptable risk. • Appropriate safety/toxicological information needs to be provided to enable WHO to develop a hazard assessment for the active ingredient and a risk assessment for the final product. When available, WHO may use a hazard assessment by a stringent regulatory authority to inform its own assessment. • New active ingredient(s) should preferably be registered by a stringent regulatory authority.
Safety – environmental effects, including disposal	• Use, disposal or degradation of the product should not pose an undue environmental hazard. • A biodegradable product would be preferable.
Non-target species	• Risks to non-target species should be in accordance with required environmental and ecotoxicology standards at the time of submission for registration.

Parameter	Preferred product characteristic
Product quality and durability	
Residual chemical content and continued efficacy	• The product should have sufficient quality and durability to provide protection from malaria infection and/or disease for at least three months in the field. • For products containing one or more active ingredients, the concentration(s) should be sufficient to induce the intended effect throughout the product's useful life and to reduce the risk of selection for insecticide resistance.
Physical durability	• The product should be UV stable and able to withstand wear and tear associated with accommodation in basic shelters, increased mobility and potential overcrowding of the target population for at least three months.
Shelf life & storage	• The product should remain fully effective and otherwise retain its quality during shipment and after storage under field conditions for up to 24 months.
End user suitability	
User acceptability	• No characteristics (such as irritancy or foul odour) should deter the user from employing the intervention. • Easy to deploy by operators, peripheral health or aid workers, and easy to adopt and maintain/use by the target population. • Not requiring a fixed structure for the application/use of the intervention is seen as an advantage. • Using an intervention design that is familiar to the target population is seen as an added advantage.
Portability	• The ability to move the intervention with the at-risk population would be preferable. Such flexibility is particularly relevant for mobile displaced populations.

REFERENCES

1 Malaria control in humanitarian emergencies: an inter-agency field handbook. 2nd ed. Geneva: World Health Organization; 2013 (https://apps.who.int/iris/handle/10665/90556).

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