DESIGN
OF EPIDEMIOLOGICAL TRIALS FOR VECTOR CONTROL PRODUCTS

REPORT OF A WHO EXPERT ADVISORY GROUP

CHÂTEAU DE PENTHES, GENEVA,
24–25 APRIL 2017

World Health Organization

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GLOSSARY

Public health value: A product has public health value if it has proven protective efficacy to reduce or prevent infection and/or disease in humans.

Efficacy: An intervention measured when it is implemented under ideal, highly controlled circumstances; efficacy is typically measured in phase III studies.

Effectiveness: The degree of benefit of an intervention measured when it is delivered and used operationally under routine, "real-world" conditions; effectiveness is typically measured in phase IV studies.

1. EXECUTIVE SUMMARY

The World Health Organization (WHO) is mandated to provide guidance to Member States on matters of public health policy, including evidence-based policy recommendations for new vector control interventions. To that end, the Vector Control Advisory Group (VCAG) advises WHO on the value to public health of new vector control tools, including new products, technologies and approaches, intended to protect humans against pathogens transmitted by vectors. WHO recommends products for use in public health based on demonstrated evidence of their impact on diseases as well as safety and quality, but must reconcile the requirements for robust data to assess public health value with the urgent need for new tools to address critical threats (e.g. insecticide resistance and spread of Aedes-transmitted viruses). In response, WHO has called for an Expert Advisory Group (EAG) to review trial methodologies for evaluating data on the impact of new tools to prevent and control vector-borne diseases.

The recommendations developed by consensus of the Group emphasized the importance of randomized trials with robust study designs. Specific recommendations are provided on end-points, design considerations, and generation of evidence on the efficacy of long-lasting insecticidal nets (LLINs) that incorporate a non-pyrethroid class of insecticide (either alone or in combination with a pyrethroid insecticide) and on products that use indoor residual spraying (IRS) of insecticides with a novel entomological mode of action (e.g. slow-acting insecticides or insect growth regulators), which differ from the insecticides currently used for public health. The outcomes of this meeting will be used to inform the development of a WHO manual on trial designs for evaluating new vector control tools that are currently not covered by a WHO policy recommendation, for publication in 2017.

2. BACKGROUND

In accordance with WHO's mandate to provide guidance to Member States on matters of public health policy, the Organization develops evidence-based policy recommendations for new vector control tools, technologies and approaches. In 2012, an independent advisory body – the WHO Vector Control Advisory Group (VCAG) – was established to advise the Organization on the evaluation and validation of the public health value of new vector control tools, including new products, technologies and approaches, used to protect humans against pathogens transmitted by vectors.[1] VCAG reviews the potential of all new tools that target transmission of vectors-borne pathogens, such as those that transmit malaria and many neglected tropical diseases. The Group is jointly managed by the WHO's Global Malaria Programme and the Department of Control of Neglected Tropical Diseases.

Because WHO recommendations for new tools can have far reaching effects on disease control and prevention, these must be based on clear demonstration of protective efficacy through epidemiological outcomes. For example, WHO policy recommendations for malaria vector control[2] are based on robust evidence demonstrating that use of interventions such as LLINs[3] and IRS[4] reduces disease burden (morbidity and mortality). Consequently, countries have adopted these recommended interventions as part of their malaria control strategies, and this has contributed to massive declines in malaria incidence and mortality.[5]

For any new vector control tools in new product classes, WHO requires evidence from at least two well conducted, randomized controlled trials with epidemiological outcomes and follow up over at least two transmission seasons.[6] With limited funds available for disease control, Member States are required to implement the most effective interventions for their local context. Epidemiological trials should therefore be conducted in different entomological and epidemiological settings[7] in order to verify the public health value of the new product class or product variation. Two trials is the minimum number needed to assess generalizability.

Robust data are essential to assess the public health value of new product classes and to provide operational guidance. The type and extent of these data must be carefully balanced with the urgent need to make products available expeditiously to address threats

[1] The evaluation process for vector control products [Information note dated June 2017]. Geneva: World Health