Bias & Neglect

Public Health Insecticides & Disease Control

A call for new investment, new policies and better advocacy

Africa Fighting Malaria Policy Paper – December 2008

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Summary

Insecticides are a vital component of disease control. To a great extent the modern insect-borne disease burden of hundreds of millions of human infections results from failures to use the chemicals we characterize as public health insecticides (PHIs). The modern arsenal of PHIs is antiquated and limited to just 12 insecticides, most belonging to just one class of insecticides (pyrethroids). The process of becoming antiquated occurs as a result of failure to invest in research and development of new PHIs. In reality, both the failure to make safe and effective use of PHIs and the failure to develop new and more effective PHIs are due to environmental opposition, limited valuable markets, considerable regulatory hurdles and weak public health advocacy; conditions which prevail even now. Indeed, even as disease control spending by aid agencies increases by orders of magnitude, disease rates may increase as investment in insecticides is neglected. United Nations agencies such as the World Health Organization (WHO), donor nations, the private sector, and research foundations should urgently prioritize investment in the search for new PHIs, as well as support advocacy efforts to promote the use of safe and effective man-made chemicals in disease control programs.

Africa Fighting Malaria is calling on the WHO, donor agencies, and other stakeholders to:

- Dramatically increase funding into the search for insecticides specifically designed for disease vector control;
- Undertake a regulatory impact assessment to establish the additional and unintended costs of new anti-insecticide regulations, with emphasis on how new regulations impede development of new PHIs;
- Address and reform the regulatory and in-country registration procedures that discourage investment in PHIs;
- Consider legislation to create incentives for the development of insecticides for public health;
- Invalidate the World Health Assembly resolution 50.13, which calls on countries to reduce reliance on the use of insecticides for disease control. Pass a new resolution establishing the importance of insecticides in disease control and calling for new public and private investment in PHIs;
- Invest in training and employing scientists, entomologists, and public health professionals skilled in vector control in countries endemic for vector borne diseases, particularly malaria and dengue;
- Recognize that PHIs have modes of action other than toxicity and that these play a vital role in disease control; and
- Support advocacy efforts to communicate and explain the urgent need for new PHIs, reduce the barriers to their deployment, and better represent the voices of people at risk from insect-borne diseases.

Unless all stakeholders invest considerable effort to create the right set of incentives for the development of new vector control insecticides and for investment in the personnel to use these insecticides, any talk of malaria elimination will remain the lazy rhetoric of public health advocates and politicians.

Introduction

According to a well known idiom, prevention is better than cure. This is invariably true for insect-borne diseases. The only proven and consistent method of insect-borne disease prevention (where vaccines do not exist) is vector control – suppressing contact between disease-spreading vectors (mosquitoes, flies, lice, and other insects) and humans in order to interrupt disease transmission.

Vector control is the most important method of prevention for diseases such as malaria, dengue and filariasis. Of the major insect-borne diseases, only yellow fever has an effective vaccine that is currently in use. However, even where a vaccine is effective and available, insufficient vaccination rates can lead to disease outbreaks, which require vector control for containment. The 2008 outbreak of yellow fever in Brazil should act as a reminder of the importance of sustaining comprehensive disease control programs that include robust vector control.[1] Outbreaks of West Nile Virus in the United States and Chikungunya in Italy act as further reminders of the need for sound and responsive vector control around the world. Insecticides remain the most important element in control of malaria and other important insect-borne diseases. Indoor residual spraying (IRS), insecticide-treated bednets (ITNs), including long-lasting insecticidal nets (LLINs), and control of mosquito larvae are proven vector control interventions that rely heavily on safe, effective, and long-lasting insecticides.

The goal of IRS is to spray the walls or ceilings of dwellings with a PHI to break contact between humans and disease vectors. While many less commonly used insecticides will kill the mosquito, thereby interrupting disease transmission, other insecticides also repel and/or irritate mosquitoes, providing a highly effective chemical screen that is proven to break man-vector contact and prevent disease transmission.[2]

ITNs and LLINs are impregnated with synthetic pyrethroid insecticides. This chemical has an irritant effect on mosquitoes, with the potential to kill if the mosquitoes rest long enough on the net. Once irritated by the pyrethroid, the mosquitoes are more likely to leave the house without biting and transmitting disease. Pyrethroids are the preferred and WHO-recommended chemical class of insecticides for bednet impregnation due to their irritating and toxic effect on insects, and their safety for humans who come into close contact with them.[3]

Larval control using chemicals such as temephos (an organophosphate pesticide) has been implemented in some limited specific settings. The expense of conducting larval control with chemicals in most malarial regions where mosquito breeding areas are widespread and diverse precludes this intervention; however, it does have, along with improved drainage, an important role to play, particularly in urban settings.

Effective vector control, as described above, requires insecticides. Without these man-made chemicals, malaria control would be limited in scale and scope. In order to sustain insect-borne disease control well into the future, we must ask ourselves: how do we ensure the continued use of insecticides for disease control and how do we encourage research and development to bring new, safe and effective chemicals to market?

Public Health vs. Agricultural Insecticides

DDT is the most effective PHI ever used. This chemical has saved millions of lives in the past and continues to save lives as part of IRS programs today. However, pressure against the use of DDT in public health programs and against the use of man-made chemicals altogether in disease control has hampered malaria control efforts and probably contributes to the lack of investment in new PHIs.

Since DDT's debut in the international arena against typhus and other insect-borne diseases during WWII, no insecticide has been developed for the primary purpose of disease

control. All PHIs were first developed and commercialized by privately-owned companies for agriculture or some other part of the domestic market; though some publicly-funded research may, in some cases, have contributed to the discoveries. Only later were a few of these agricultural pesticides adapted for use in control of human diseases. However, the public health and agricultural sectors require substantially different properties and modes of chemical action. Agricultural insecticides are designed to be short acting and have a narrow activity spectrum, while PHIs need long-lasting residual action and a broader spectrum of chemical activity. Agricultural insecticides will tend to act on the insect's stomach after it has ingested a crop, while PHIs will act as a contact poison after the insect has landed on a wall or other material.

Public health accounts for a very small fraction of the overall global market for pesticides. A review of public health pesticide products by The Boston Consulting Group for the Bill and Melinda Gates Foundation estimates that the total public health market in 2006 was worth approximately $750 million, of which $400 million is attributable to the pesticides themselves, and $350 million is attributable to the netting material used in ITNs and LLINs.[4] The same report includes an industry estimate that the total market for agricultural plant protection products is approximately $30 billion.[5] On this basis, the public health market for pesticides comprises approximately 1.3 percent of the total pesticide market.

There is little profit in PHIs and therefore little incentive for private companies to develop new and effective public health chemicals. As noted by the WHO as early as 1975, "The number of new pesticides received in 1975 for evaluation by WHO for use in vector control was considerably lower than in previous years. The great increase in the cost of developing and testing new chemical pesticides has caused industry to limit the number of compounds being developed to those which can be shown to have wide potential use in agriculture as well as in public health."[6]

Over the last two decades, very few new insecticides have been developed and formulated that can be used for vector control. Environmental regulations have taken some insecticides from the market, increasing the reliance of the public health sector on a limited number of chemicals, which can hamper vector control efforts. Furthermore, the increased cost of development, often caused by increasingly burdensome regulations and registration procedures, means that private companies target their products for the agricultural market where they can recoup their costs and make a profit. According to the Gates Foundation/Boston Consulting Group, "The global AgChem industry has been facing intense market pressures over the last decade – increasing R&D [research and development] costs, rising regulatory hurdles, price pressures, and the slowing growth of the pesticide market. R&D costs have risen 500 percent over the last 20 years…"[7]

Only 12 insecticides, from four chemical classes, are currently recommended by the WHO for IRS. According to the Insecticide Resistance Action Committee, "the most recent "new" compound made available for vector use is etofenprox which was commercialized in 1986, and even this did not possess a distinct mode of action."[8]

A 2005 report for the WHO Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) recognizes that "there would be substantial benefit from the availability of new insecticides."[9] However, the report goes on to state, "any development of new insecticide for use to protect humans is likely to be as secondary use for a product developed primarily for agricultural purposes."[10] This unfortunately amounts to a re-statement of the status quo and provides no insight into how innovation might be spurred to bring a new PHI to market.

Insecticide Resistance

Since almost all classes of PHIs are still used in the agricultural sector, vector species

experience prolonged exposure to insecticides. The widespread use of insecticides for agricultural and public health purposes increases the probability that resistance will build up. When vectors breed in close proximity to agricultural crops, they are exposed to the same or similar insecticidal compounds and thus develop resistance.[11,12] Many vector species of public health importance have developed resistance to one or more insecticides.[13]

Insecticide resistance poses a major threat to vector control. Mosquitoes' prolonged exposure to an insecticide over several generations increases their ability to survive after coming into contact with that insecticide. Mosquitoes can produce many generations per year allowing resistance to develop quickly. In some cases, insecticide resistance has been documented within just a few years of the insecticide being introduced. According to the Centers for Disease Control and Prevention, "there are over 125 mosquito species with documented resistance to one or more insecticides."[14] Though toxic resistance to DDT has been noted, to a large extent it is an exception to other insecticides. Even after decades of public health use, DDT is still one of the best and most widely used chemicals for preventing malaria transmission inside houses. It has a powerful spatial repellent action to prevent the selection of resistance in mosquitoes when used for malaria control.[15] In fact, DDT is the only chemical recommended for malaria control that stops mosquitoes from entering houses and transmitting disease.[16]

In light of the Roll Back Malaria Partnership's (RBM) recent call to massively scale-up the distribution of ITNs and LLINs, pyrethroid resistance is of particular concern. Increased resistance would inhibit the effectiveness of these interventions by allowing mosquitoes to enter and/or bite through the nets. There is growing concern that extensive use of ITNs and LLINs could contribute to the spread of insecticide resistance. A recent study found signs of pyrethroid resistance in a western Ugandan district where free pyrethroid treated bednets have been distributed since 1998.[17]

Pyrethroid insecticides are also used in IRS. A study in Benin compared the impact of pyrethroid resistance on the efficacy of IRS and ITNs. A reduction in efficacy was seen in both interventions.[18]

For several decades, WHO reports warned of the development of insecticide resistance among disease vectors.[19] During the 1970s, WHO reports called for "research related to the development and improvement of attack measures against the vector, at both larval and imago stages."[20] A report of the Seventh Asian Malaria Control Conference in 1982 prioritized the need for new vector control compounds "in view of the urgent need for new insecticides."[21]

Then in 1999, a WHO Bulletin reported:

> As a result of cross-resistance [resistance to an in-use insecticide that confers resistance to another insecticide that is not in use] due to the *kdr* gene (16, F. Chandre et al., unpublished data, 1999) there is an urgent need for alternatives to the currently available pyrethroids. In this regard, WHOPES (WHO Pesticide Evaluation Scheme) has a major role to play. Collaborating centres need to be revived, priority being given to those working on malaria vectors in areas where *A. gambiae* s.l. has already developed resistance to pyrethroids. Collaboration with agrochemical companies should also be stimulated to ensure that any useful existing insecticide will not be withdrawn from the market and that the search for new insecticides will be actively encouraged.[22]

A year later the Global Collaboration for Development of Pesticides for Public Health (GCDPP) Working Group, which was established by the WHO Pesticide Evaluation Scheme (WHOPES), "unanimously recognized the urgent need to pursue development of

alternative pesticide products for vector control...The Group noted that the investment of pesticide industry in R&D of vector control insecticides is inadequate."[23]

Anti-Insecticide Agenda

Not only has there been little action behind the statements made by the WHO, the backlash against the use of DDT in agriculture has led to the emergence of an institutional bias against insecticide-focused interventions for public health, as well as an activist campaign. In 1993, the Pan American Health Organization's (PAHO) *Pesticides and Health in the Americas* prohibited "the use of pesticides that are included in the Dirty Dozen of the International Pesticide Action Network."[24] Pesticide Action Network (PAN) is a network of environmentalist groups whose goal is to "replace pesticide use with ecologically sound and socially just alternatives."[25] It is surprising and of concern that PAHO, a UN body, would directly adopt the agenda of a non-government environmentalist organization; but this would not be the last time this would happen.

In 1997, a World Health Assembly (WHA) resolution called on member states to "take steps to reduce reliance on insecticides for control of vector-borne diseases through promotion of integrated pest-management approaches in accordance with WHO guidelines, and through support for the development and adaptation of viable alternative methods of disease vector control."[26] The resolution does not explain what such alternative methods might compose, but typically they would include 'environmental management' and the use of larvivorous fish.

During the discussion and debate of the resolution at the WHO Executive Board Meeting in January 1997, the Chairman of the session called on Consumers International, a group which represents the interests of Western consumers and was known to be hostile about DDT, to make arguments in favor of the resolution and against the use of DDT in disease control. There is no record of representation or arguments from scientists involved in insect-borne disease control, disease control program managers, or citizens of the countries affected by insect-borne diseases.[27]

The internal dissonance continues today. The WHO justifies reduced reliance on insecticides and adoption of integrated vector management on the fact that "the arsenal of insecticides is limited, and there are few prospects for new candidate compounds coming to market."[28] The arsenal of malaria *treatment* is also limited due to drug resistance; however as a result, the WHO does not pursue a policy of reducing reliance on medicines to treat malaria. Rather the WHO and other partners work to improve malaria case management as well as develop new and effective treatments. The same policies should hold for insecticides, which as a preventive measure, should be prioritized.

While the WHO and some donors may well acknowledge and support the use of insecticides when used on treated materials, such as LLINs, there is an institutional bias against the use of insecticides in IRS programs.[29] Bias against IRS was seen recently in a factually inaccurate press release issued by the WHO Regional Office for Africa (AFRO) directly attributing the success of the Southern African Lubombo Spatial Development Initiative (LSDI) to LLINs.[30] However, the cornerstone of the LSDI has been a carefully planned and comprehensive IRS program, which has been documented in numerous reports and scientific literature. The inaccuracies in this press release were explained to the WHO AFRO by Africa Fighting Malaria, but no retraction was issued and WHO AFRO continues to mislead the media and public on the true successes of the LSDI program.[31]

Additionally, organizations like PAN continue to advocate for malaria prevention methods such as improved sanitation and water drainage as alternatives to chemical spraying and to the use of DDT in particular. On World Malaria Day 2008, PAN addressed a letter to the US Agency for International Development

(USAID) expressing their concerns about USAID's funding of IRS programs and their support of DDT.[32] PAN's actions directly undermine the WHO Global Malaria Program's call in 2006 for an expansion of IRS programs and for DDT to be used in malaria control.[33] PAN also stresses the importance of community involvement in combating malaria. Community involvement and buy-in is important and has been a feature of the USAID-led President's Malaria Initiative (PMI). Indeed, community acceptance of IRS in areas such as Zanzibar is extremely high - over 90 percent - and is in fact higher than that of ITNs.[34]

The desire of PAN and other environmentalist groups to 'replace pesticide use with ecologically sound and socially just alternatives' may resonate well with some who are anxious about the use of man-made chemicals. However, such approaches usually focus on the potential risk posed by man-made chemicals and ignore the very real and deadly risks posed by disease-spreading insects. The definition of a 'socially just alternative' is unclear but surely it should be determined by the people living with malaria and other insect-borne diseases and should be based on the risks *they* face.

The calls for 'ecologically sound' methods of malaria control are not new. A 1979 Report of the WHO Expert Committee on Malaria discusses progress in developing biological controls such as larvivorous fish, microbial agents, genetic control, and environmental management. Despite their somewhat optimistic assessment of these alternative methods, these technologies remain unproven and are very limited in their usefulness for malaria control, which still relies on man-made chemicals for vector control.

The Search for New Public Health Insecticides

The Gates Foundation/Boston Consulting Group analysis found it could take up to 10 years and $300-400 million to bring a new class of insecticides to market.[35] The RBM's Global Malaria Action Plan (GMAP) estimates that a new active ingredient would require an investment of more than $175 million over 12 years.[36] Much of the high cost of developing new PHIs is due to the burdensome and capricious nature of the regulations governing insecticides. A regulatory impact assessment is needed to determine to what extent these regulations are stifling research and development of new PHIs. Such an impact assessment should not only estimate the increased cost of bringing a new chemical class to market, but should estimate the number of lives that are lost due to the burdensome regulations that many governments and UN agencies have put in place.

While the RBM's GMAP report calls for more investment in the development of new public health pesticides it notes "the public health market for pesticides is very small compared to that of the agriculture market, and therefore receives much less investment and research focus."[37] While this statement may be true, RBM and its partners provide no practical way forward or vision for the development of PHIs, as was seen previously with the WHO CIPIH.

Some may have hoped for new investment and commitment to develop PHIs when the Stockholm Convention on Persistent Organic Pollutants came into force in 2004. This Convention, designed to ban or restrict the use of persistent pollutants (which includes DDT), encourages parties "within their capabilities, to promote research and development of safe alternative chemical and non-chemical products, methods and strategies for Parties using DDT…"[38] In 2002, Dr. John Buccini, Chair of the Intergovernmental Negotiating Committee of the Stockholm Convention, wrote, "All Parties to the Convention are committed to developing alternatives to the pesticide [DDT]. The situation will be reviewed within one year of the Convention entering into force, and every three years thereafter, to see when DDT production and use may be eliminated. Considerable research and development efforts by all the world's countries will be needed if suitable alternatives are to be developed and implemented in a timely

way."[39]

The Global Environment Facility (GEF), a global financing partnership established to address environmental problems, is the interim financial mechanism of the Stockholm Convention. Since its establishment in 1991, it has provided grants of $7.4 billion and has attracted co-financing from partner organizations of $28 billion for various 'environmental' programs and projects.[40] In 2006, 32 donor countries provided $3.13 billion to the GEF for projects between 2006 and 2010.[41] Despite this substantial funding, the GEF's investment into the search for alternatives to DDT has been disappointing.

To date, GEF has only provided $37 million (0.5 percent of total grants provided) and secured a mere $47 million in co-financing from partner organizations (0.17 percent of total co-financing provided) "in support of DDT alternatives."[42] Closer examination of GEF funded projects reveals that little or none of these funds would be devoted to the search for chemical alternatives to DDT. GEF funded projects have focused mainly on biological controls, environmental management, ITNs and "combination[s] of the above with supportive insecticide use."[43]

A GEF project approved in 2005 aimed to "demonstrate cost-effective, environmentally sound, and locally appropriate alternatives to DDT for malaria vector control, ensuring their sustainable use through strengthened national and local capacity for malaria control"[44] in three African countries (Eritrea, Ethiopia and Madagascar). The background documents for this project state, "other countries such as Angola, Botswana, Mozambique, Zambia and Zimbabwe previously relied on DDT and now mainly rely on alternative insecticides" and "will be invited to participate in the project in order to share their experiences in transitioning to other chemicals..."[45] Ironically, since this document was prepared, Mozambique, Zambia and Zimbabwe have returned to using DDT in malaria control[46,47,48] and according to the PMI, Angola's Ministry of Health is currently considering the use of DDT along the Namibian border.[49]

Despite paltry public funding for alternatives to DDT and almost no allocation of these funds for chemical alternatives to DDT, the Conference of Parties (COP) to the Stockholm Convention and the Stockholm Convention Secretariat remain determined that all uses of DDT will be eliminated by 2020.[50] It was not until the third meeting of the COP in 2007 that a decision was made to establish a plan to promote a partnership to develop alternatives to DDT. Then in November 2008, the Convention Secretariat convened a meeting of stakeholders to discuss the plan.[51] That this meeting of stakeholders occurred four years after the Convention came into force and seven years after the agreement of the final text provides no evidence of the commitment to find alternatives to DDT that John Buccini referred to. Furthermore, given the GEF's poor record in funding alternatives to DDT and the expense and obstacles inherent in developing a new class of chemicals that could be used in public health, it is unlikely that this business plan will lead to new chemical alternatives.

Aside from a $50 million grant from the Bill and Melinda Gates Foundation to the Innovative Vector Control Consortium (IVCC), no new investment of any significance has been made in the search for PHIs. Compare that with the roughly $425 million committed to the PATH Malaria Vaccine Initiative, tasked with finding a malaria vaccine.[52,53] Additionally, funding for new insecticides is approximately 20 percent of the estimated $238 million donated to the Medicines for Malaria Venture, a public private partnership geared to developing new malaria treatments.[54]

The IVCC is an important and highly valuable consortium. Nevertheless, there is a profound and urgent need to fund many more research projects and to far greater levels in order to develop new PHIs and make them available to public health programs. Perhaps the greatest shortfall of past and present PHI research and development efforts has been failure to focus on the multiple modes of chemical actions (especially non-contact repellent and contact irritant actions) that serve to interrupt human-vector contact and prevent disease transmission inside houses.

The limited funding for new PHI development is matched by regulatory regimes that discourage new chemical development. Many private companies face considerable hurdles in registering their products in malarial countries. Slow and opaque registration procedures penalize investors, especially those that have developed a product for a niche market, such as public health. The delays and expense of a slow registration process encourage private companies to focus purely on those markets, such as crop protection, in which they are more likely to recoup their costs and make a profit.

Regulations from developed nations discourage investment even more. For instance, the European Union (EU) is currently debating draconian new legislation that would change the way that agricultural pesticides are assessed in the EU. The EU is proposing a move away from risk-based assessments of chemicals toward a hazard-based approach. Risk-based assessments evaluate the real world application of chemicals and their risk to humans and the environment. Hazard-based assessments establish 'cut-off criteria' that would reject chemicals based purely on laboratory data regardless of their actual risk to humans or the environment. It would be unscientific to adopt a hazard-based approach, as it would ignore the age-old observation by the scientist Paracelsus that 'the dose makes the poison.' Around half the number of chemicals ever tested is known to be carcinogenic, yet it would be absurd to call for the banning of these products, which would include wine, beer and a host of foods happily consumed by people every day. Cut-off criteria would include endocrine disruption, which is controversial and poorly defined, and would create a regulatory environment that is uncertain and arbitrary.

Although the EU regulations only deal with agricultural pesticides, many of these chemicals, such as pyrethroids and carbamates, are currently used in disease control and could well be withdrawn from the market entirely if their use in the agricultural market is curtailed or eliminated. Around 170 malaria scientists and public health experts have signed a letter of petition to the European Parliament and European Commission registering their concerns and objections about the proposed regulations.[55]

While the EU appears ready to impose unscientific and capricious new regulations on pesticides, improved regulation of PHIs is desperately needed from the WHO, and in particular from WHOPES. The creation of the GCDPP was a start; however a review of their reports demonstrates that while they have discussed the need for new pesticides, little has been done to generate investment and action in this regard. The GCDPP was established "to strengthen WHOPES activities, [and] to facilitate the search for alternative safe and more cost-effective pesticides."[56] Yet according to the GCDPP's 2008 report, WHOPES has only tested and evaluated one product for IRS and two products for long-lasting treatment of bednets since September 2006.[57] Furthermore, it should be noted that the product under review for IRS (Fenitrothion CS) is not a new insecticide but rather a new formulation of an old and widely-used insecticide.

WHOPES can only test products that industry brings forward, but as a WHO body, it could be more proactive and aggressive in advocating for better policies that encourage research into PHIs. Although WHOPES has been criticized as being slow and somewhat unresponsive to the needs of public health communities, it fulfils an important and necessary role.[58] WHOPES does not consider itself a regulatory agency, but it is seen as a de-facto regulator by many malarial country governments that lack the expertise and infrastructure to provide clear, predictable and fair regulations.

The Way Forward

Malaria control has benefited from public campaigns in the US and EU to raise money for LLINs and to raise awareness of the disease through popular television programs such as American Idol and MTV. But there is almost no popular advocacy or advocacy targeted at

policy-makers for insecticide development. The participation of celebrities is valuable in raising money for LLINs - a critical component of most malaria control programs. However, the interests of people living in malarial areas may be better served in the long run if these celebrities came out more generally supporting all uses of insecticides, including IRS, and spoke out about the need to develop new PHIs. Challenging the stigma created by modern environmentalist groups to man-made chemicals will be an important component in efforts to fund and support the development of new chemical classes for disease control.

Despite WHO's call for more IRS, there remains a severe lack of leadership within global public health institutions with respect to insecticides. Almost all malaria control programs rely on insecticides for the treatment of bednets, IRS and/or larval control. In the real world, most malaria control programs in highly endemic countries can only make use of PAN-promoted insecticide-free methods, such as environmental management, in urban areas or in very limited and specified situations. Thus, the PAN-promoted methods leave vast numbers of people grievously exposed to the extraordinary risks of debilitating and fatal diseases.

In recent years, several countries have re-started or expanded IRS programs to great effect. However, these programs depend in large part on methodologies and equipment developed during the 1940s. New and effective insecticides for ITNs, LLINs and IRS are sorely needed. There is an urgent need to broaden grassroots support for the infrastructure of malaria control and the tools required to save lives now and well into the future. This must proceed from a stronger advocacy component for the application of insecticides as well as the development of new ones.

That there has been such a dearth of public funding for PHIs is probably due to the successful and aggressive advocacy of environmentalist groups against the use of man-made chemicals in disease control as well as a lack of effective advocacy and leadership for the use of insecticides from the malaria control community. The lack of profitability in PHIs is also found with medicines and vaccines for malaria and other tropical diseases. However, with support from several governments, the WHO and major donors, hundreds of millions of dollars have been invested in the search for new medicines and vaccines. Public-private partnerships have been established and a dynamic research agenda has been pursued with promising results.

The same highly enlightened system of public and private financial support along with incentives should be developed for PHIs. Such incentives should include legislation to encourage private investment in insecticides specifically designed for public health. For instance, legislation that mirrors the Food and Drug Administration's Orphan Drug Act or Priority Review Voucher could be introduced for the insecticide market. Both are designed to encourage investment in products for diseases that would otherwise not be profitable. Fast-track regulatory reviews for new agricultural products could be granted for any company that successfully develops a novel and appropriate chemical for disease vector control.

While rich-country governments can and should address the barriers that discourage investment and create incentives for new investment, malarial country governments must urgently review their regulatory and registration procedures so that these do not discourage investors and chemical manufacturers. At the same time, WHO, donors and other UN agencies should ensure that WHOPES is more responsive to the needs of the broader public health and scientific community. WHOPES should broaden its mandate by recognizing that chemical actions other than toxicity (e.g. non-contact repellent and contact irritant actions) are needed for preventing man-vector contact and disease transmission. The de-facto role of WHOPES as a regulator for many malarial country governments must also be recognized

and on that basis, reforms enacted so that it can fulfill its role better. A key element would be for WHOPES to receive the funding and resources so that it can take on the important and valuable role that it should play in the development and regulation of PHIs.

An important element for private companies interested in the development of PHIs would of course be the prospect of long-term support for malaria control. Therefore, donor agencies as well as malarial country governments should commit themselves to supporting malaria control and clearly communicating their support for comprehensive disease control, including IRS and larval control where appropriate.

Attempts to encourage investment in new PHIs are currently undermined by the WHA resolution 50.13, which calls on member countries to reduce their reliance on PHIs. This creates uncertainty for investors and also undermines the current efforts of the PMI, RBM partners and others to scale up malaria control programs. Resolution 50.13 will continue to be used by activist groups to limit the use of insecticides. The WHO along with the major donors and stakeholders involved in malaria control (as well as control of other insect-borne diseases) must act urgently through the WHO Executive Board and the WHA to invalidate this resolution. At the same time, the malaria community, including scientists, donors and advocacy groups, should push for a new WHA resolution. Such a resolution would establish the importance of insecticides to public health programs and would call for substantial public and private investment in new PHIs.

Insecticide resistance management is crucial to ensure effective and sustainable vector control. Countries should be encouraged to work on insecticide resistance mitigation and management strategies. However, to do this effectively, new public health chemicals are needed and staff must be deployed on the ground to plan, implement and monitor the most appropriate and rational use of these chemicals. There is a serious deficit of trained malaria scientists and medical entomologists in most malarial countries. Effective resistance management requires trained professionals to understand vector biology; donors and malarial country governments must prioritize the training and employment of the next generation of public health professionals, without which effective resistance management and sustained malaria control cannot take place.

Lastly, the scientific community must recognize that modes of action other than toxicity are beneficial to disease control. This should become common knowledge through evidence-based research, which requires funding agencies to acknowledge that varying chemical characteristics exist with the potential to reduce transmission of disease.

Conclusion

Taxpayers in the developed world are actively supporting the fight against insect-borne diseases, notably malaria. Malaria is widely acknowledged to be a good 'public health investment' and some early evidence from Africa, the region most affected by malaria, suggests that in some countries, the disease burden is falling. However, it is highly likely that funding for malaria control is not being sensibly allocated, since so little is going toward the development of insecticides - the primary component in disease control. While the search for an effective malaria vaccine has consumed many millions of dollars over several decades, the public health community is still many years away from a product that can be deployed. During this time, almost no public or private funding has been allocated to search for a new and effective insecticide specifically designed for malaria control. One could point to the lack of profitability in this market as the underlying cause for the lack of investment. However, the worrying lack of leadership from the WHO and donor agencies along with the persistent anti-insecticides advocacy from environmentalist groups has undermined the search for solutions. Few advocacy groups, scientists or policy makers will oppose investment in the search for a malaria vaccine or new treatments. However, vocal

public support and advocacy for investment in PHIs has been missing while environmentalist groups have actively opposed the use of man-made chemicals in disease control.

It is incumbent on UN agencies, donor nations, the private sector and philanthropists to challenge the status quo and create a regulatory and financial environment that encourages investment in new vector control insecticides. This will entail support for advocacy work that will be required to explain the importance of man-made chemicals in the fight to save lives from preventable diseases such as malaria. For too long aggressive and well-funded advocacy efforts have undermined the use of man-made chemicals in disease control, encouraged ever more onerous regulations, and failed to represent the interests of people at risk from insect-borne diseases. Unless considerable efforts are undertaken by all stakeholders to create the right set of incentives for the development of new vector control insecticides and for the investment in the personnel to use these insecticides, any talk of malaria elimination will remain the lazy rhetoric of public health advocates and politicians.

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