



August 31st, 2018

Response by the MSF Access Campaign to the consultation on IACG Discussion Paper **'Reduce unintentional exposure and the need for antimicrobials, and optimize their use'**

The MSF Access Campaign welcomes the opportunity to contribute to this critically-important dialogue on antimicrobial stewardship. While commending the efforts of the IACG Working Group in producing this Discussion Paper, in the section below, we directly address a number of ambiguities and omissions in the document that we request be addressed in its subsequent revisions.

- i) **Quote:** *'Good guidance is available: There is a wealth of good, relevant guidance that, if put into practice, would lead to a significant, rapid reduction in the inappropriate use of antimicrobials in humans, animals and plants.'* (page 1)

Response: With respect to antimicrobial use in human populations this is only partly true. There are some forms of 'guidance' that have the potential to lead to a reduction in such inappropriate use – particularly training for health professionals in distinguishing between aetiologies and severities of infectious illnesses, along with evidence-based clinical guidelines for antimicrobial prescriptions – but the availability of such tools in remote populations and low-resource settings is typically very limited. That, combined with the limited range of antimicrobial medicines available in such settings, means that a broad-spectrum, empirical approach to therapy is often required that relies on selection from a narrow range of agents. We must also acknowledge these constraints and develop 'guidance' tools particular to healthcare in severely resource-limited settings.

As the degree of stewardship capacities vary significantly between and within countries, recommended measures to optimize use must reflect on the abovementioned limitations and adopt tools relevant for each of the **tiers of the stewardship** system.

- ii) **Quote:** *'Infection prevention and control measures, supported by adequate water and sanitation infrastructure, will make a difference: Significant WASH improvements and effective strategies to change practices are essential, combined with the application of biosecurity measures.'*

Response: This quote, and the sections in the document devoted to the topic of infection prevention and control (IPC), focus almost entirely on WASH and neglect to address the critically-important role of vaccination, both in human and animal populations (acknowledging that the latter is outside MSF's particular expertise). Given the strong and growing evidence for vaccines as a safe, sustainable and cost-effective means of preventing infections, there should be more clear recommendations regarding vaccines in the paper.

- iii) **Quote:** *'Harmonized approaches to regulation are essential: To ensure effective, science-based regulation on AMR, and to avoid trade friction elicited by different regulatory approaches to AMR, countries must be encouraged to take a harmonized approach based on international standards.'*

Response: The relevant sections of the current draft of the paper focus on 'unnecessary or suboptimal use of antibiotics' as seen from the perspective of informal markets, and also the problem of substandard or falsified medicine. Absent from the discussion regarding legal and regulatory systems is the need to address the phenomenon of irresponsible manufacture and marketing of antimicrobial products, whereby pharmaceutical companies make spurious or inappropriate claims regarding the efficacy and clinical indications for their products and/or manufacture antimicrobials in combinations that are unnecessary, potentially harmful and contribute significantly as drivers of AMR. The nature and magnitude of this on prescriber, supplier and patient behaviours is poorly understood and will need to be a key area of study and work in the regulatory domain.

Some specific responses to the ‘**Open questions for stakeholders**’ posed on the last page of the Discussion Paper are as follows:

- *What kind of support (other than financial) is needed to translate the existing guidance into implementable actions?*
 - Large-scale technical support will be required to develop locally-relevant, epidemiologically-informed clinical guidelines for appropriate antibiotic use.
 - Technical assistance in addressing shortfalls in the legal and regulatory capacity to develop and enforce regulations regarding appropriate antibiotic manufacture, supply, distribution and consumption in many countries.
 - Costing analyses of interventions to mitigate AMR on the various levels, informed by pilot case studies can assist countries in prioritizing and tailoring the interventions based on their varying starting point and the expected outcomes.
 - Similarly, more case studies on successful interventions on AMR from resource-limited settings are needed. This information will be useful in informing local decision-makers on the most effective measures.

- *How can policy makers be assisted to further develop and implement infection prevention and control in human and animal health and plants and be convinced to invest now to mitigate the escalating and future costs and obtain benefits far beyond preventing AMR?*
 - Every effort should be made to identify and adapt existing tools for use in suitable settings, rather than investing time, energy and financial resources into unnecessarily developing new materials.
 - Mainstreaming interventions on AMR across multiple, currently siloed programmatic areas while looking for specific AMR results is recommended. This can amplify the activities' outreach and increase buy-in among healthcare professionals as well.
 - Surveillance data are essential for understanding the magnitude of AMR and therefore convincing policy makers of the need to invest upfront. Further, such surveillance data should be kept updated and provide information that is ‘actionable’ for practitioners in terms of making visible particular local dynamics and trends of resistance that can be taken into account in prescribing practices.

- *What incentives or initiatives are needed for behaviour change towards responsible use in the health sector (hospitals, community health centres) and in the food and animal production sectors (animal and plant health professionals, food producers and manufacturers, consumers).*
 - In hospitals and health facilities, the focus should be on education and training of health professionals to better understand the role of antimicrobials and inform their patients appropriately
 - Engaging and educating community leaders is a key lever in successfully informing the public regarding the optimal use of antimicrobials
 - More research is needed to understand reasons behind the insufficient deployment of economic and social incentives to achieve behavior change on various levels of healthcare system.

- *What approaches are needed to ensure the industry and investors manufacture and market antimicrobials responsibly, and not stimulate overuse or contribute to environmental pollution?*
 - This touches on the point raised above about irresponsible, unethical and/or dangerous marketing practices and links to the need to **regulate** against such harmful practices on the part of pharmaceutical manufacturers.

- *Changing practices needs the support of the industry - how can we balance the availability of a public good such as effective antimicrobials, with a private industry perspective?*
 - There is a clear need for binding regulations to be agreed at a global level in order to both guide the actions of private industry in a manner that optimises public health objectives; and sets a level playing field for these actors.
 - Regulations should be agreed at the supra-national level, but since binding regulations are the sole responsibility of governments, enforcement will need to take place at the national level. Governments will require mechanisms to hold each other to account in this regard.
 - Given the significant conflicts of interest that emerge from the private sector's involvement in the antibiotic lifecycle - from manufacturing sites to the bedside of a patient, it is inappropriate to include private industry in the formulation of regulatory standards or in overseeing their implementation and enforcement.

- Research has exposed unethical practices which both directly and indirectly drive the emergence of resistance¹. However, more understanding is needed in their scope, particularly in resource-poor settings where health system limitations allows for unregulated, third-party involvement.
- *What are the mechanisms to enhance the availability and utility of global resources for the end user (communities and individuals) to optimize or reduce the need for the use of antimicrobials and mitigate the unintentional exposure to the environment?*
 - Reduce the price of vaccines and scale up their use: In addition to the essential tools required to diagnose infections and treat them appropriately, a further key to reducing antibiotic resistance is to prevent infections in the first place. Increasing affordable access to vaccines should be a high priority within the global AMR response. Vaccine coverage remains unacceptably low in many countries where MSF works despite the overwhelming evidence supporting vaccination as an effective, low-cost measure to reduce the burden of both infectious diseases and AMR at every level². For example, it has been estimated that introduction of Haemophilus influenzae type b (Hib) conjugate vaccine and pneumococcal conjugate vaccine (PCV) to 75 developing world countries could reduce antibiotic use for these diseases by 47% and avert 11.4 million days of antibiotic use in children younger than 5 years old each year³. Other vaccines for diarrhoeal and respiratory infections, in particular, have similar potential.
 - Currently, vaccination coverage is unacceptably low in many countries where MSF works. PCV, to take one example, remains unaffordable for a number of LMICs. By May 2018, globally 53 countries (27%) had not introduced a PCV vaccine in their national immunisation programme⁴. Of these 53 countries only 7 are Gavi-eligible countries⁵, which illustrates a trend seen for years whereby low-income countries are introducing new vaccines at a faster pace than middle-income countries (MICs) due to the availability of international donor financial support. The lowest price of ~USD 10 per child is available to those countries that are subsidised by Gavi, the Vaccine Alliance and, since 2017, to humanitarian organizations through the Humanitarian Mechanism, a mechanism for accessing affordable and timely supply of vaccines for use in humanitarian emergencies. Even some Gavi-supported countries are not scaling up PCV coverage

¹ WHO/ Health Action International Collaborative Project, 'Understanding and Responding to Pharmaceutical Promotion, A Practical Guide', First Edition working draft for Pilot Field Testing, <http://haiweb.org/wp-content/uploads/2015/05/Pharma-Promotion-Guide-English.pdf> Accessed 30th August 2018

² Kathrin U Jansen & Annaliesa S Anderson (2018): The role of vaccines in fighting antimicrobial resistance (AMR), Human Vaccines & Immunotherapeutics, DOI: 10.1080/21645515.2018.1476814

³ Laxminarayan R, Matsoso P, Pant S, Brower C, Røttingen JA, Klugman K, Davies S. 2016. Access to effective antimicrobials: a worldwide challenge. Lancet 387:168 175.doi:10.1016/S0140-6736(15)00474-2

⁴ WHO Data, statistics and graphics, http://www.who.int/immunization/monitoring_surveillance/data/en/ Accessed 5th July 2018

⁵ IVAC's digital platforms contain downloadable vaccine introduction maps : <http://view-hub.org/viz/> Accessed 5th July 2018

in their immunisation programmes for fear that they won't be able to sustain an affordable supply once they transition out of Gavi funding and have to pay much higher prices. Global funds such as Gavi, the Vaccine Alliance have been set up by donor governments to support the role out and uptake of much needed medical tools such as vaccines. However, in recent years these funds have insisted on 'transitioning' or 'graduating' middle-income countries out of eligibility for support. As such the usefulness of these funds to address the access issues of a wider range of countries is diminished. The IACG should recommend that any mechanism to expand access to AMR-related health technologies, including vaccines, be global in scope. This could start with revisiting and reversing the current trend towards restricting support for LMICs through 'graduation' and 'transition'.

- Moreover, governments must be supported to address situations of monopolies and high prices where these are barriers to access for needed AMR technologies- drugs, diagnostics and vaccines. This involves avoiding the granting of poor quality patents as well as making use of compulsory licensing to overcome unaffordable prices of monopoly products. Given the unaffordable prices of certain important medical tools that have been shown to reduce the need for the use of antimicrobials, this should be a priority for the IACG.
- If unchecked, **antibiotic shortages** can endanger availability of critically-important antibiotics on a global scale. Addressing issues influencing sustainability of antibiotic supply chain, including lack of producers, extremely centralized production systems, and the need to attract generic manufacturers to produce antibiotics, is central to comprehensive solutions.
- Pooled procurement, as specifically modelled by the Global Drug Facility (GDF), should be explored as a key mechanism for ensuring both lower prices for antibiotics and improved stewardship. The GDF represents a large portion of the market for TB drugs and diagnostics, and uses this to negotiate prices with companies based on larger volumes. GDF's international tenders allow both generic and innovator companies to compete in supplying quality-assured TB health products. It rejects tiered pricing; encourages suppliers to enter into markets; provides forecasting to suppliers as well as providing governments with forecasting assistance and orders (which is important given different shelf lives). It anticipates and addresses global supply issues and provides advice to countries on switching to optimal from sub-optimal formulations. In the area of diagnostic tools, GDF has been able to negotiate improved service and maintenance terms from companies.
- Data generation is essential to diagnose the contours of the problem of availability. **Need to measure access** to antimicrobials - which is a largely unexplored area particularly in settings where MSF operates - is therefore key. Efforts to collect data on consumption should be

complemented with measuring access to first and second-line antibiotics. Similarly, there is a critical need to scale up the body of evidence on access to antibiotics on a country level, including via the use of assessment tools to measure access and develop country case studies and making this data publicly available through publication and submission to global repositories.