ReAct briefing

WHA74 Agenda point 17.3:

Pandemic Prevention, Preparedness and Response (PPPR) and antibiotic resistance

The Covid-19 pandemic has clearly exposed the limitations of global collaboration within existing global health structures, pointing to a need for more rules-based global governance as well as massive efforts to strengthen health systems to prevent, prepare and respond to health emergencies in a more just, equitable and effective way.

1) Include antibiotic resistance in the scope of PPPR

If a proposal for a new global framework for PPPR – such as the proposal for a 'Pandemic Treaty' - is advanced by governments at the WHA74, it should avoid adopting a narrow focus on viral pandemics similar to COVID-19. While more viral pandemics may likely come in the future, the global community must be able to prevent and respond to global cross-border health threats more broadly. Antibiotic resistance, although not a disease as such, is an obvious example of a global cross-border health threat affecting countries in pandemic proportions. Currently, antibiotic resistance causes 750,000 annual deaths globally. If left unchecked, it threatens to unravel basic and modern medicine with crippling effects on health systems in all countries. As antibiotics are also widely used for animals and plants in food and agriculture production systems, both the drivers and the impacts of antibiotic resistance are broader and more complex than for Covid-19. Decades of funding neglect, combined with continuously increasing global antibiotic consumption, poor surveillance data, and weak pipelines for new drugs, vaccines and diagnostics, has left the world dangerously vulnerable to a pandemic of resistant and untreatable infections.

Against this background it is important to ensure that antibiotic resistance is included in the scope of a potential new global PPPR framework with the aim to ensure sustainable access to *effective* antibiotics for all.

2) Pandemic prevention, preparedness and response and antibiotic resistance: Areas in common

The zoonosis aspect and the need for a One Health approach

New pathogens arise in the interface between humans and animals. As seen with SARS-CoV-2 and other pathogens before, new variants of pathogens or even completely new pathogens arise in the interface between humans and animals - both wild and domesticated. Antibiotic resistant strains of bacteria are no different - new versions, with mutations that can render existing antibiotics useless are likely to arise in environments where animals are crowded together and antibiotics are used - often excessively.

One such example was the discovery in 2015, that bacterial resistance to a last-resort antibiotic - colistin - had become mobile. Through so-called "horizontal gene transfer" the resistance gene '*mcr-1*' could cross species barriers and enter bacteria dangerous to both humans and animals. Just two years later, it had been found in more than 30 countries across 5 continents and had spread to healthy human and animal gut, and started to cause deaths from treatment failure in bloodstream infections. Investigations showed that it had most likely originated in pigs. Addressing antibiotic resistance, just like future viral pandemics, requires taking a cross-sectoral 'One Health' approach in mitigation and prevention strategies.

The need for improved global surveillance for both viral and bacterial infections

Global surveillance and rapid testing is essential for detecting disease outbreaks early and monitoring their developments, as well as identifying mutations early and monitoring their spread. This is a crucial element in understanding the global spread of Covid-19, as well as for antibiotic resistance as noted above in the *mcr-1* example.

However, surveillance and capacity for monitoring resistance development is weak and uneven, particularly in LMICs. The 2020 report from WHO's Global Antimicrobial resistance Surveillance System showed that while the US and Germany were able to submit resistance data from more than 44,000 and 16,000 surveillance sites respectively, the number of surveillance sites from the whole of the African and South-East Asian regions were only 93 and 110, respectively. The report also noted a huge difference in the quality of data submitted, and the number of patients that pathogens were isolated from - ranging from over 800,000 patients to just 19 per country. Such uneven capacity for surveillance is an Achilles heel of global preparedness for emerging pandemics.

Support for increasing laboratory capacity, strengthening surveillance and monitoring systems in LMICs, and developing integrated analysis of data across the human, animal and environment sector that account for *both viral and bacterial threats,* should be a key priority under a global PPPR framework. It should build on already existing systems, included the increased capacity built under Covid-19. Importantly, as it is crucial to share pathogen data, a global framework needs to ensure that any *obligations* to share are adequately matched with equally strong *rights* to access to medical products (or other benefits) that may emerge as a result of such data-sharing and availability.

The need for a health-needs driven research and development model

The lack of effective prevention and treatment options at the outset of the Covid-19 pandemic has once again highlighted the need to address the shortcomings of the market-based pharmaceutical research and development system, which is both unsuited and inefficient for developing biomedical tools of big public health value, but which have a limited or unknown commercial market.

Access to effective antibiotics is critical in any pandemic preparedness and response, yet no new classes of antibiotics have been discovered in over three decades due to an overreliance on a market-driven R&D model. A 2021 analysis by the WHO showed that out of 43 candidates in clinical development, *only two* compounds target the multidrug-resistant bacteria of biggest global concern.

A global PPPR framework should be able to address the shortcomings of the current R&D model. Crucially it should be able to:

- Establish global prioritization and coordination of R&D activities and funding relevant for PPPR, including for antibiotics (where a global Priority Pathogens List already exists to guide investments).
- Take an end-to-end approach, i.e. be able to address bottlenecks from the earliest stages of R&D all the way down to production, procurement and distribution.
- Ensure improved sharing of research knowledge and transparency of data at all stages to improve efficiency and accelerate scientific progress.
- Improve capacity and establish mechanisms for public health management of intellectual property, technology and knowhow. Clear common rules and procedures should be established for the effective and swift operation of such mechanisms.
- Ensure full inclusion of all countries, as well as the prioritization of vulnerable populations e.g. pregnant women and children, in innovation and R&D. R&D capacity is increasing in many LMICs and they should be involved in pre-clinical and clinical R&D, manufacturing, production and distribution to create a sustainable system for the future.

Increasing transparency and strengthening of global pharmaceutical supply chains

Global shortages of PPE, oxygen, vaccines and drugs continue to have serious consequences in the current pandemic, including for antibiotics that are used to treat secondary bacterial infections that can arise as complications in Covid-19 patients. Increasing events of antibiotic shortages have been reported during the Covid-19 pandemic with a tenth of all drug shortages listed by the US FDA in June 2020 being for antibiotics.

Antibiotic shortages are a serious problem affecting both high, middle and low-income countries. Shortages can lead to worse treatment outcomes for patients, when they are forced to use alternatives that may be less effective or have side-effects. Shortages are caused by a number of factors linked to production interruptions, trade restrictions, fragile - sometimes even single source - supply chains as well as fragmented and unpredictable procurement practices and systems.

A global PPPR framework should:

- improve transparency in global pharmaceutical supply chains.
- create regional diversification of active pharmaceutical ingredient production and product production capacity.
- streamline procurement practices for essential biomedical tools such as antibiotics, for example through pooled procurement mechanisms.

Ensuring equitable, affordable and timely access to health commodities

Vaccine-nationalism, and reliance on a donation-based approach to access, has led to grossly inequitable access to life-saving vaccines globally, despite political intentions otherwise and massive public investments to support and expedite their development. Similarly lack of access is also a major problem for new antibiotics despite large public investments. In 2020, it was shown that 40% of new antibiotics in late-stage development lack access plans. New antibiotics are also registered in just a few countries per year. Going forward, public R&D investments must be leveraged to achieve far better outcomes.

- A PPPR framework (and the financing that should come with it), should be used to transform the global R&D system to become more coordinated, collaborative and driven by public health needs.
- A new system should ultimately be able to deliver and manage 'global public goods' - such as effective antibiotics - that are affordable and accessible to everyone in need in a timely and sustainable manner. This inevitably means addressing how increased public leverage over IP can be created to ensure it is managed in a public health friendly manner.
- Sustainable and affordable access can only be ensured if addressed already at the inception of any R&D project and throughout the whole R&D process, whether for antibiotics, other therapeutics, diagnostics or for vaccines. This is most effectively done by attaching conditions on public funding, and creating a system of delinkage to finance R&D. Waiting until a product is in late-stage clinical development or has received regulatory approval to start addressing access is far too late, as has clearly been shown for Covid-19 vaccines, as well as for new antibiotics.

3) Specificities to account for relating to antibiotic resistance

Stewardship - access without excess

All use of antibiotics drives resistance development (both correct and incorrect use), which is why unnecessary and incorrect use must be avoided as much as possible. That the use of a certain medicine leads to its decreased effect is a unique challenge in global health. The need to avoid their overuse to preserve them is something which makes antibiotics different from other medicines and vaccines. At the same time, lack of access to effective antibiotics worldwide likely causes more deaths than antibiotic resistance itself. For these reasons, specific measures must be considered for antibiotics, to not only expand affordable access, but balance their availability against the need to avoid misuse and overuse. Access without excess is needed.

This aspect goes against what presumably will be a key goal of a pandemic preparedness and response framework, namely ensuring rapid, equitable and broad access to needed medical supplies at surge demand. The need for antibiotic stewardship must however be accounted for. Increased efforts to strengthen health systems and increasing universal health coverage should be seen as central elements to ensure access to antibiotics without excess. Money invested today will pay off many times over in times of crisis.

4) Modalities of negotiations for a global framework

Regardless of the form that a global PPPR framework eventually will take, ReAct believes that the following considerations are imperative for making negotiations productive and fruitful:

- Negotiations must be inclusive of all LMICs. The timing and process must also ensure that all countries are able to fully participate in the negotiations.
- Special interest groups such the pharmaceutical industry, foundations and others should be consulted as any other affected stakeholders, but *not* form part of any advisory body or negotiation structure.
- And finally, while negotiations should be able to deal with Covid-19 in the short term, they must be able to also focus on the long-term ie. addressing known and potential drivers and structural causes of future outbreaks, epidemics and pandemics.