

'The Pandemic Treaty' and antibiotic resistance



The Covid-19 pandemic has exposed the limitations of global collaboration and response within existing global health frameworks, pointing to a clear need for more rules-based global governance to be able to effectively prevent, prepare and respond to health emergencies in a more just equitable way. With the recommendation to proceed with the establishment of a new legal instrument to the upcoming WHA Special Session, ReAct believes that the following considerations are imperative for making negotiations of a new legal instrument 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 as the pharmaceutical industry, private foundations and similar bodies should be consulted as any other affected stakeholders, but should not form part of any advisory body or negotiation structure.
- While negotiations should be able to deal with Covid-19 in the short term, a new legal instrument must be able to focus on the long-term i.e. addressing potential drivers and known structural causes that may lead to future outbreaks, epidemics and pandemics.

Include antibiotic resistance in the scope of a pandemic treaty

A legal instrument should avoid adopting too narrow a focus on viral pandemics similar to Covid-19. More viral pandemics will no doubt emerge, but governments should significantly bolster global and national capacity 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 which already affects countries in pandemic proportions. Currently, antibiotic resistance causes 1.27 million annual deaths across the globe with far-reaching consequences. Increasing resistance to existing antibiotics is already showing signs of its potential to unravel basic and modern medicine with crippling effects on health systems. Misuse and overuse of antibiotics by humans, animals and plants in food and agriculture production systems, exacerbates the problem. 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.

Several elements of an effective global system for pandemic prevention, preparedness and response are in common with what is needed to addressing antibiotic resistance, including:

- Developing medical countermeasures and new antibiotics both require a health-needs driven research and development model.
- Pandemic prevention and preparedness and addressing antibiotic resistance both require taking a One Health approach.
- Improved global surveillance are required for both viral and bacterial infections.
- Increased transparency of global pharmaceutical supply chains and strengthening regional production capacity.
- Ensuring equitable, affordable and timely access to health commodities.

1. Developing medical counter-measures and new antibiotics both require a health-needs driven research and development model

A new global legal instrument should be able to address the shortcomings of the current R&D model. Crucially it should be able to:

- Establish global prioritization, coordination of R&D activities and long-term funding for R&D relevant for pandemic preparedness and response, including for antibiotics.
- Take a comprehensive end-to-end approach to innovation, i.e. be able to address bottlenecks from the earliest stages of R&D all the way down to production, procurement, distribution and patient access.
- Improve global sharing of research knowledge and transparency of data to improve efficiency and accelerate scientific progress.
- Establish well-functioning clinical trial networks that can bring down costs and ensure products are tested, where the need is greatest
- Ensure full compliance with established ethical standards for clinical trials are followed incl. clear requirements to provide access to end-products in countries, where the trials are run.
- Establish mechanisms for public health management of intellectual property, technology and knowhow. Clear operating rules and procedures should be outlined in the legal instrument 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.

2. Pandemic prevention and preparedness and addressing antibiotic resistance both require taking 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 pathogens and their variants arise in the interface between humans and animals - both wild and domesticated. Antibiotic resistant strains of bacteria are no different - new mutations that can render existing antibiotics useless are likely to arise in environments where animals are crowded together, where antibiotics are overused, and where hygienic conditions are often deficient.

Bacterial resistance to a last-resort antibiotic - colistin - became mobile

In 2015 for example, it was discovered 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 started to cause deaths due treatment failure in human bloodstream infections. Investigations showed that it had most likely originated in pigs with un-regulated food supply chains and untreated water facilitating its global spread. Addressing antibiotic resistance, just like future viral pandemics, requires cross-sectoral 'One Health' collaboration.



3. Improved global surveillance are required for both viral and bacterial infections

Global surveillance and rapid testing are essential for detecting disease outbreaks early and monitoring their developments, as well as identifying mutations and monitoring their spread. Improved surveillance is crucial 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, educated personnel, 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.

4. Increased transparency of global pharmaceutical supply chains and strengthening regional production capacity

Global shortages of personal protective equipment, oxygen, vaccines and drugs have had serious consequences in the current pandemic. Similarly, report of antibiotic shortages have increased during the Covid-19 pandemic in both HICs and LMICs – one tenth of all drug shortages listed by the US FDA in June 2020 were for antibiotics. Shortages can lead to worse treatment outcomes for patients when alternative treatments may be less effective or have side-effects. Shortages are caused by a number of factors linked to production interruptions, trade restrictions, unsustainable - sometimes even single source - supply chains as well as fragmented and unpredictable procurement practices and systems.

A new legal instrument should deliver greater transparency in global pharmaceutical production capacity and in global supply chains. Creating more regional diversification of active pharmaceutical ingredient production and product production capacity will be essential. A new legal instrument should also establish clear procurement practices for essential drugs, such as antibiotics, for example through global or regional pooled procurement mechanisms.

5. 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 financial investments to support and expedite vaccine development. Similarly lack of access is also a major problem for new antibiotics despite considerable public investments. In 2020, it was shown that 40% of new antibiotics in late-stage development lack access plans. Newer antibiotics are only registered in just a few countries per year.

Going forward, public R&D investments must be leveraged to achieve far better outcomes, including by:

- A new legal instrument (and the financing that will support it) should transform the global R&D system of medical countermeasures to deliver '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 increased public leverage over intellectual property to ensure it is managed in a public health friendly manner.

- Sustainable and affordable access can only be ensured if taken into account at the inception of any R&D project and throughout the whole R&D process. 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.

Specificities to account for relating to antibiotics

Stewardship

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. At the same time, lack of access to effective antibiotics worldwide likely causes more deaths than antibiotic resistance itself – for now at least. For these reasons, specific measures to not only expand affordable access to antibiotics, but balance their availability against the need to avoid misuse and overuse. Ensuring access without excess.

This requirement may be at odds with what presumably will be a key goal of a new legal instrument: facilitating timely access for all to medical countermeasures in times of crisis. The need for antibiotic stewardship must however be accounted for even in times of crisis. 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.