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Ellen 't Hoen PhD, LLM., Director Medicines Law & Policy

Thank you for inviting me to the European Parliament STOA workshop on Tackling antimicrobial resistance: from science to policy.

My name is Ellen 't Hoen, director of Medicines Law & Policy and Global Health Law fellow at the law faculty of the University of Groningen.

As part of a comprehensive package of measures to combat antimicrobial resistance (AMR), it is paramount that new classes of effective antibiotics are developed. The last new class of antibiotics that made it to the market was discovered in 1984 and development pipelines for truly new classes of antibiotics are all but empty.

Antibiotics are a special class of pharmaceuticals that do not fit the pharma industry's standard business model. This pharma business model is based on selling as much as possible for as long as possible and at the highest price the market will bear. The ability to charge high prices is sustained in the European Union (EU) by a generous system of market exclusivities, including patents and exclusivity rights that are granted through the medicines regulatory system. Such exclusivity rights create market monopolies and, as a result, enable high medicines pricing.

New antibiotics, however, need to be reserved and used cautiously while assuring their availability for patients who need them, else they too risk becoming less effective due to antimicrobial resistance. In other words, the pharma industry would have to be persuaded to leave the new antibiotic drugs mostly on the shelf to be used sparingly.

The industry will not invest in developing health products they cannot sell, and therefore large pharmaceutical companies have abandoned the search for new antibiotics. Smaller companies have entered the field but struggle with raising the cash because the mega-profit prospect isn't there. In other words, the current pharmaceutical research and development (R&D) model fails to deliver in this field.

The need to craft different incentive models for new antibiotic drug development has been recognised for years and has been the subject of numerous reports and policy proposals, including a U.K. government-commissioned report by the economist Jim O'Neill published in 2016.

Central to his proposal to encourage the development of new antibiotics are so-called 'market-entry rewards.' O'Neill recommended an award of around $1 billion each to the developers of successful new drugs, subject to certain conditions to ensure that the new antibiotic drugs are not "overmarketed" and yet are available to patients who need them wherever they live. That was the carrot. He also proposed a stick in the form of a "play or pay" funding scheme in which companies must pay a modest levy on the sale of their existing medicines into an international or regional fund unless they can demonstrate they are investing an equivalent amount in antibiotic R&D.

Not much has happened with his recommendations and the European Commission is now pursuing an entirely different route, and it is one O'Neill did not favor.

In the recently leaked draft of the revision of the EU's pharmaceutical legislation (Articles 40-42), the Commission proposes so-called transferable data exclusivity vouchers (TDEV) to incentivize antibiotic drug development. A company that applies for marketing authorization with the European Medicines Agency for a "priority antimicrobial" can obtain a transferable data-exclusivity voucher. Such a voucher provides an extra year of data exclusivity, which amounts to one year of extra market monopoly either for the antibiotic registered or another product authorized for use in the EU. The company applying for the voucher needs to demonstrate its ability to supply the EU market in sufficient quantities and provide information on all funding received related to the development of the antimicrobial. The voucher can be transferred (sold) to another company and be transferred an unlimited number of times. The EU voucher scheme would be in force for 15 years, during which period a maximum of 10 vouchers may be granted (subject to extension upon proposal by the Commission).

So far, this is the proposal and it has not been formally published.

But many have raised concerns:

In practice, this would mean that generic competition for the product to which the voucher is applied will be delayed for the duration of the extended exclusivity period of one year. Needless to say, the generic industry is not keen on the proposal. They point out that it will increase the cost to health care systems dramatically. For example, extending the exclusivity period for adilumimab (Abbvie's Humira), a product used to treat arthritis, would have meant an additional cost of 1 billion euro ($1.1 billion) for the EU's health care systems. It would also introduce uncertainty for the generic industry as to

when they can enter the market with generic or biogeneric versions of a product when such a product may be subject to an extended period of market monopoly.

O'Neill addressed the shortcomings of the voucher system in his 2016 report: *"[Vouchers] push the cost of antibiotic development onto an arbitrary set of payers and patients (those who use the medicines on which the voucher is applied). Secondly, to deliver a similar incentive for new drugs, compared to market entry rewards, these vouchers would cost the healthcare system more in the long-term as they have to reward the innovative drug developer and provide an additional profit margin to the company selling the drug on which the voucher is applied."*

A recent Lancet commentary shared similar concerns: a 1-year voucher could cost the European health care systems up to 3 billion euro ($3.2 billion) and would decrease access to medicines due to delayed market entry of generic medicines. The authors mention that studies have shown that similar incentive mechanisms may have accelerated market entry of products that are already in late-stage development but have done little to enhance R&D in the neglected areas. Vouchers also do not ensure access to new antibiotics because companies may choose not to supply certain markets or seize activity. The draft legislation permits the Commission to revoke the voucher when supply, procurement, or purchase criteria have not been fulfilled, but only before its transfer. The voucher scheme also has no link between the clinical value of the new antibiotic and the reward given, since that is determined by the value of the product to which the voucher is applied. Instead of implementing a voucher scheme, the commentary's authors propose subscription-style payments at EU level that guarantee income to those who develop antibiotics delinked from the amount of product sold. For additional commentary also see this forthcoming paper in the Journal of Law, Medicines, & Ethics.

The industry will certainly be interested in extending the monopolies on some of their blockbuster drugs by buying vouchers. The vouchers, after all, are tradable. But is it the most sensible way to address antibiotic drug development?

Fourteen EU Member States spoke out against TEVs because they are "an indirect non-transparent form of financing that stifle innovation and block generic competition."

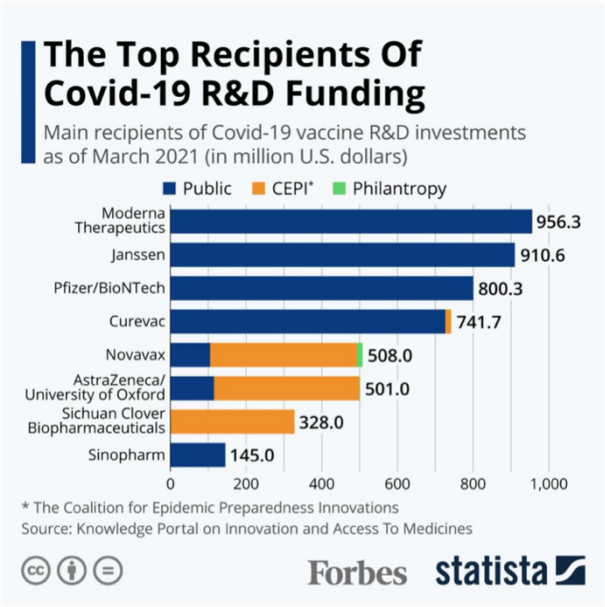
A similar proposal for exclusivity vouchers has been proposed in the US but has thus far failed to gain support in the US Congress.

So what would be a better approach?

There are lessons to be drawn from Covid-19. These include:

Medicines Law & Policy

Public financing of Covid Vx



Main recipients of Covid-19 vaccine R&D investments as of March 2021. STATISTA

1- Direct funding of R&D and procurement including, advance market commitments made the rapid development of Covid-19 vaccines happen (not the generous exclusivity system). This slide above shows the top recipients of Covid-19 vaccine funding. This public financing secured the rapid development of vaccines for a disease that a little over three years ago was hardly known. A similar approach should be taken for antibiotic drug development. The global health crisis that is upon us as a result of antimicrobial resistance most certainly justifies a similar level of financial commitment.

2- Antimicrobial resistance and the funding of the development and regulation of new antibiotics requires an international approach - one not dissimilar to the negotiations of a new pandemic treaty currently taking place at the World Health Organization. In antibiotic drug development, global equitable access to new medicines should also be an important central concern. We know from Covid-19 vaccines that without deliberate action this will not happen.

3- The UN High Level Meeting on AMR in June of this year should lead to concrete actions and money on the table. There are sufficient declarations of good intend - it is time to go beyond that. It is the Commission's mission to " work with [our] international partners to advocate for a global agreement on the use of and access to antimicrobials." The UNHLM is an opportunity to advance this.

4- There is a strong role for European Health Emergency Preparedness Response Authority (HERA) in preventing the AMR crisis from further spinning out of control by direct investing in the development of new antibiotics and collaborate in this internationally. HERA already funds work in this area for example the not-for-profit Global Antibiotic Research and Development Partnership (GARDP).

One final thought: It might be worth dusting off O'Neill's "play or pay" proposal to finance the new innovation models. After all, companies are making huge profits from infectious diseases. Covid-19 revenues amounted to close to $100 billion in 2022. It is not an unreasonable proposal to reallocate some of those resources - generated by public spending - to antibiotic drug development. Even a modest skimming would generate a meaningful fund for antibiotic drug development.

Last but not least: It would be important for the Commission to publish its plans for the revision of the pharmaceutical legislation as requested today again by civil society organisations.