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Review on Antimicrobial Resistance

Tackling drug-resistant infections globally

PRESS NOTICE **14 May 2015**

Jim O'Neill sets out plan to overhaul the global antibiotics pipeline

Our arsenal of antibiotics is losing its effectiveness against drug-resistant bacteria, the so called 'superbugs'. Yet the new medicines we need are not being developed fast enough.

In a report published today, Jim O'Neill's Review on Antimicrobial Resistance sets out proposals to overhaul the global antibiotics pipeline over the next ten years. This is one in a series of reports by the O'Neill Review, before their final recommendations by the summer of 2016.

The report identifies the reasons why commercial investment is lagging in this area and recommends three types of targeted interventions:

1. **Commit lump-sum payments to successful drug developers to support a viable market for the highest priority antibiotics**. A global body would make payments that incentivise the development of the most needed antibiotics to combat rising drug resistance. This approach 'de-links' the profitability of a drug from its volume of sales: it reduces the commercial imperative for a drug company to sell new antibiotics in large quantities, which can contribute to the development and spread of drug resistance.
2. **Jump start a new innovation cycle in antibiotics by getting more money into early stage research.** A global antimicrobial resistance (AMR) Innovation Fund of around 2 billion USD over 5 years would help boost funding for blue-sky research into drugs and diagnostics, and get more good ideas off the ground.
3. **Catalyse discoveries into new drugs by supporting the antibiotics development process throughout the R&D pipeline.** Innovative partnerships at early development stages between academia and industry, public bodies facilitating clinical trials, or lowering financial and regulatory barriers to successful drug development could all play a role to catalyse antibiotic discovery.

The O'Neill Review on Antimicrobial Resistance estimates that possibly as little as 16 billion USD, and no more than 37 billion USD over ten years could achieve a substantially revitalised pipeline of four major new breakthrough antibiotics (and a number of important 'follow-on' products). This amounts to a one-off cost increase to the global market for antibiotics (currently worth about 40 billion USD annually) of less than 10%, with the cost spread over a decade. These sums pale in comparison with the cost of AMR: according to the US Center for Disease Control, antibiotic resistance costs 20 billion USD to the United States alone every year in excess healthcare costs.

Jim O'Neill and his team will spend the coming 12 months engaging with governments, NGOs and pharmaceutical companies globally to discuss and develop these proposals further, with input from an international advisory group. They will present a more detailed package of actions by the Summer of 2016.

While action to stimulate the development of new antibiotics will be a decisive step forward in the global battle against AMR, the report is clear that this represents just a single part of the solution to the diverse challenges of increasing drug resistance. Decisive action is also needed to change the way that antibiotics are used and misused in humans, animals and the wider environment. The Review will publish further papers over the course of 2015 looking at critical issues that contribute to this, including the use of antibiotics in agriculture, the potential for new diagnostic technologies to improve the way that doctors prescribe, and the scope for replacing some of our antibiotics usage with alternative ways to fight infections, such as vaccines or new therapeutic approaches.

Quotes about the report

Jim O'Neill, Chairman of the Review on AMR, said:

"No new classes of antibiotics have been created for decades and our current drugs are becoming less effective as resistance increases.

We need to kick-start drug development to make sure the world has the drugs it needs, to treat infections and to enable modern medicine and surgery to continue as we know it. My Review on AMR has today published clear proposals to supercharge antibiotics discovery, potentially saving millions of lives for a fraction of the 100 trillion USD cost of inaction"

Dr Manica Balasegaram, Executive Director, Access Campaign, Médecins Sans Frontières, said:

"This timely report highlights the fact that we have major gaps in needs-driven R&D that affect rich and poor countries alike. Bold interventions such as de-linkage- a measure that uncouples profitability from volume of sales - are urgently needed in order to promote innovation, access and conservation of antimicrobials. A global innovation fund for AMR and key infectious diseases would also be catalytic in changing the landscape."

Severin Schwan, CEO of Roche, said:

"Innovation in antibiotic R&D is critical for enabling the development of new treatments to combat the increasing global threat of antimicrobial resistance. As the AMR Review Committee highlights, new models are needed to incentivise antibiotic discovery and development while also ensuring the appropriate controls are in place to safeguard the use of these life-saving treatments in clinical practice. The solution requires collaboration and action from pharmaceutical and

biotech companies, academia, governments and public health organisations - Roche is committed to working with the AMR Review Committee and being a part of this solution."

Patrick Vallance, GSK's President of Pharmaceuticals R&D, said:

"It is essential that we find new ways to increase antibiotics R&D and create a future pipeline of new treatments. Antibiotic resistance is a hugely complex problem with potentially devastating consequences for public health. As one of the few companies still conducting research in this area, we welcome today's report. We are very encouraged by the ideas it sets out to modernise the economic model to encourage investment in research and ensure reasonable returns for successful innovation while discouraging unnecessary use of new antibiotics. We look forward to working closely with the AMR Review Team and others to take these ideas forward."

Kenneth Hillan, Chief Executive Officer of Achaogen, said:

"The AMR report highlights an important set of initiatives to keep pace with the rise of antibiotic resistance. We welcome the AMR's call for a more predictable market for antibiotics, to sustain future commercial investment in R&D and their urgent call for global innovation funding for research. Despite the costs involved in many of these initiatives, the price of inaction – whether measured by lives lost or increased healthcare costs – is far greater."

Dame Sally Davies, Chief Medical Advisor to the UK Government, said:

"This latest report will stimulate important conversations between Governments, pharmaceutical companies and other funders. We have to respond to the challenge of AMR by making sure we secure the necessary antibiotics for generations to come, in order to save millions of lives and billions of pounds."

Notes for Editors

1. AMR is the term used to describe drug-resistant infections, sometimes referred to as 'superbugs'. Antimicrobials include antibiotics, antivirals, antiparasitics and antifungals.

2. The Report, *Securing new drugs for future generations: the pipeline of antibiotics*, will be published on the Review's website at www.amr-review.org on Thursday May 14th.

3. The UK Prime Minister, David Cameron, commissioned the Review on Antimicrobial Resistance in July of last year to address the growing global problem of drug-resistant infections. It is Chaired by Jim O'Neill and backed by the Wellcome Trust and the UK Government.

4. Jim O'Neill is an internationally published economist and until 2013 was Chairman of Goldman Sachs Asset Management, having previously been the organisation's Head of Economic

Research. Before chairing the Review on Antimicrobial Resistance he led the Cities Growth Commission which played a central role in the Government's decision to devolve significant new powers to large urban centres in the UK starting with Manchester and the Northern Powerhouse project. He is particularly well known for his work in relation to developing and middle-income economies, having coined the BRIC (Brazil, Russia, India, China) acronym – meaning that he is especially well-placed to understand the broad range of international interests raised by antimicrobial resistance.

5. We are pleased to announce that Sanjeev Chaudhry of India, Mike Bonney of the United States and Dr Ren Minghui of China have agreed to join a new international advisory group to the Review on AMR. More details are available on the Review's website (www.amr-review.org).

6. The Wellcome Trust is a global charitable foundation that spends more than £700 million a year on advancing human and animal health. It is the second highest-spending charitable foundation in the world, after the Bill & Melinda Gates Foundation, investing principally in biomedical science, the medical humanities and public engagement. The Trust is providing part-funding for the work of the Review, and hosting the team at its London headquarters.

7. An *Accelerated Access Review* has been launched to make recommendations to Government on speeding up access for NHS patients to innovative medicines and medical technologies. The review is independently chaired by Sir Hugh Taylor, with Prof Sir John Bell acting as Head of its expert advisory group and is expected to report to government later this year.

This Press Release will also be available on Thursday 14th May 2015 on www.amr-review.org.

Media enquiries should be addressed to the AMR team on: press@amr-review.org and 020 7611 5729. For out of hours enquiries please call Jeremy on +44 (0)7715 426895 or Hala on +44 (0)7715 426891.

Securing new drugs for future generations: the pipeline of new antibiotics

Executive summary

The problems and the causes of antimicrobial resistance (AMR) are diverse. In our two published papers so far, we have made the case that the potential future human and economic costs of AMR are too catastrophic to ignore; and set out five necessary steps that should be taken immediately to tackle this challenge.

In this paper, we focus on one element of the problem: the need to boost the development of new antibiotic drugs.

Our analysis of the antibiotics that have been recently approved and those at various stages of development shows a mismatch between what we know the world needs, given emerging levels of drug resistance, and the size and quality of the pipeline to address this growing challenge.

For example, there is rising resistance to 'carbapenems', a class of antibiotics that constitute doctors' last good line of defence against a range of potentially life-threatening infections such as pneumonia, and bloodstream infections. Yet perhaps only three compounds under development at the moment have the potential to be active against the vast majority of bacteria resistant to carbapenems, despite them having reached worryingly high levels in some countries already.

The main reason for this mismatch is that the commercial return for any given new antibiotic is uncertain until resistance has emerged against a previous generation of drugs. In other medical fields, a new drug is meant to significantly improve on previous ones and so will become the standard first choice for patients quickly once it comes to market. That is often not true for a new antibiotic: except for patients with infections that are resistant to previous generations of drugs, a new antibiotic is most probably no better than any existing and cheap generic product on the market. By the time that new antibiotic becomes the standard first line of care, it might be near or beyond the end of its patent life.

We set out proposals to address this problem and bring forward the financial reward to new antibiotics that address drug resistance. We think our proposals can radically overhaul the antibiotics pipeline over the next 20 years: our costs are modelled on achieving 15 new antibiotics a decade, of which at least four should be breakthrough products, with truly novel mechanisms of action or novel therapeutic profiles targeting the bacterial species of greatest concern.

First, we want to make antibiotics R&D commercially sustainable so that the field can attract the best minds from research organisations, small biotech companies, large firms or not-for-profit entities. To do that we propose a system by which a global organisation has the authority and resources to commit lump-sum payments to successful drug developers. Payment would have to be set against selective criteria agreed in advance. Such an approach would 'de-link' the profitability of a drug from its volume of sales, supporting conservation goals by eliminating the commercial imperative for a drug company to sell new antibiotics in large quantities – a key factor in contributing to the development and spread of resistance.

Creating a more stable commercial end market for antibiotics in this way will mean investment will trickle down to the earlier stages of the pipeline. But we think we should also jump-start a new

innovation cycle in antibiotics by getting more money into early stage research. A global AMR Innovation Fund of around 2 billion USD over 5 years would help boost funding for blue-sky research into drugs and diagnostics, and get more good ideas off the ground. Big pharma should have a role in paying for this innovation fund: it needs to look beyond short-term assessments of profit and loss, and act with 'enlightened self-interest' in tackling AMR, recognising that it has a long term commercial imperative to having effective antibiotics, as well as a moral one.

Finally, there are ways to further reduce barriers to drug development by lowering costs, improving the efficiency of research, and lowering global regulatory barriers wherever possible without compromising patients' safety. Much has already been done in this space but we should continue to explore ways to bring new drugs to market as quickly and as easily as possible.

These interventions will require political leadership at a global level. To work, it requires giving health authorities the means to deliver the new system, with rules in place to limit unfair free-riding by some countries or some companies. We do not underestimate the difficulty but there are examples of successful coordination in the health sector and we would like to learn the lessons of initiatives such as UNAIDS on HIV/AIDS, or GAVI on improving access to vaccines.

These interventions will also require financial resources but the cost is modest compared to the problem the world faces if AMR is not tackled. Today in the US antibiotic resistance already costs the healthcare system an additional 20 billion USD a year. In comparison, we estimate that a comprehensive package of interventions could cost as little 16 billion USD and no more than 37 billion USD over the course of 10 years and would be sufficient to radically overhaul the antibiotics pipeline. This money would only be paid out when new and useful products are brought to market, not as a taxpayer-funded subsidy upfront. Such sums amount to a one-off increase, over the course of a decade, of less than 10% on what the world today spends on antibiotics (40 billion USD a year). This is hardly a high price to pay given that antibiotics are essential to so many aspects of healthcare, from common infections to surgery and chemotherapy.

We look forward to working with governments, industry and other interested parties around the world over the next 12 months, as we develop these initial ideas further into a more detailed package of action.