

# Managing Antimicrobial Resistance Through Behavior Change, March 2021

## Roadmap for guiding the implementation of incentives to stimulate antibiotics R&D

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### Background

In 2001, when the World Health Organization recognised antimicrobial resistance (AMR) as a global health challenge and formulated a strategy to address it, the focus on the development of new drugs, among other things, evoked hope among actors engaged in combatting AMR. Today, we can see that the global response and the outcome thereof has been rather disappointing. Only three new classes of antibiotics have been launched in the last two decades, and all are outcomes of research advances made in the 1980s or earlier. Investing in the development of new antibiotics is still dubious from a commercial point of view, in addition to there being scientific challenges. The backdrop of stewardship interventions means that sales of any new drug targeting a new type of resistant bacteria need to be modest. Hence, there is a strong disconnect between the public health value of antibiotics and pharmaceutical firms' ability to get acceptable return on investments in antibiotic development.

### Approach of the workshop

The aim of this workshop was to investigate why there have mostly been, as the leader of the UK AMR Review's Lord Jim O'Neill put it, 'empty words' coming from global policymakers. The workshop focused on obstacles that have hindered the implementation of three types of well-known antibiotic development incentives: Market Entry Rewards (MERs), Milestone Prizes and Pipeline Coordinators. Hence, the aim of this workshop was not to evaluate the strengths and weaknesses of these incentives per se, but rather to identify the forces blocking their implementation. In short, MERs include financial payments to a developer or intellectual property right holder after the achievement of market authorisation of an antibiotic that meets pre-defined product criteria. Milestone Prizes are monetary rewards given to developers after

the achievement of clearly specified R&D goals, such as an approved Phase I trial, including addressing particular pathogens. A Pipeline Coordinator is a public/non-profit organisation that closely tracks the antibacterial pipeline and actively supports R&D related to priority pathogens, during the development process, deploying funding, advice, and a range of other support activities.

During the workshop, 31 participants – representing academia, global and national policy bodies, NGOs, start-ups, and the pharmaceutical industry – were asked to give their perspectives on the following issues:

- a) The current obstacles to introducing MERs and concrete ways to address these obstacles.
- b) The current obstacles to introducing Milestone Prizes and concrete ways to address these obstacles.
- c) The current obstacles to making Pipeline Coordinators permanent and concrete ways to address these obstacles.

If the identified obstacles can be characterised as varied, the suggested solutions can be characterised as 'variations on a theme': no obstacle can be resolved by any actor on its own. What is required is interactive, long-term engagement from multiple stakeholders, that is, measures coordinated across national, legal, and organisational borders. Below, we will present the identified obstacles related to each incentive, while the proposed solutions are presented in the section on recommendations.

### Market Entry Rewards

The current obstacles to introducing MERs which were mentioned in the workshop can be summarised as follows.

**Obstacles relating to Funds and Funders:** There is a lack of such international cooperation between countries and supranational bodies that would be



necessary to implement a MER of a size considered to be effective, that is, above USD 1 billion. Moreover, there are problems finding the money to pay for such an incentive on a sustainable basis. These two aspects (cooperation and money) are related and thus make up a set of obstacles which need to be addressed simultaneously.

**Obstacles relating to Design Uncertainties:** There are uncertainties regarding how to calculate the optimal size of the MER in terms of funds, how to set the conditions for receiving a MER, and how a MER would work when other mechanisms (e.g., grants) are used. These uncertainties make companies less interested in MERs, as the MER initiative is seen as overly complicated.

**Obstacles relating to Coordination and Priorities:** These obstacles refer to problems such as countries being hesitant to harmonise practices (e.g., setting prices or choosing reimbursement models for buying drugs). There is also an issue regarding who determines who gets a MER. Is this decided by the funders? Or is it done more objectively, based on where it is most needed? If so, what resistance threat should be addressed? Included in such difficulties in reaching agreement are potential conflicts of interest between funders, high-income countries, which are able to pay for the MERs, but might not need to use the newly approved antibiotics, and low- and middle-income countries, which would have problems paying for the MERs, but might have the greatest need to use the new antibiotics against local resistant strains.

## Milestone Prizes

The obstacles to introducing Milestone Prizes that were voiced in the workshop discussions can be summarised as follows.

**Obstacles relating to the perceived Cost/Benefit:** It was suggested to be hard to estimate the size of Milestone Prizes in terms of how much money developers should be given. Moreover, from the perspective of the payer, it was also seen as risky that the payer might not get value for money (e.g., if a subsidised project were not brought to completion) or that the incentive might allow low-quality products.

**Obstacles relating to Coordination:** In the discussions, the need for coordination between Milestone Prizes was seen as a particular obstacle to their implementation. Specifically, in the discussion participants saw a need to coordinate Milestone Prizes (i) across prizes, (ii) across different milestones (preclinical or clinical phases) as well as (iii) across countries.

**Obstacles relating to Agreement:** Echoing some of the obstacles to implementation of MERs, the implementation of Milestone Prizes was seen as

suffering from problems regarding where to get the money from, on the one hand, and how to prioritise needs in selecting which antibiotics to support, on the other.

## Pipeline Coordinators

The obstacles to making Pipeline Coordinators permanent that were brought up during the workshop can be summarised as follows.

**Obstacles relating to Lack of Political Stability of Priorities:** It was suggested that, in order for Pipeline Coordinators to be made permanent, the main issue would be how to fund them in the long term (more than 10–12 years). Such long-term funding was seen as difficult to achieve because continual changes in political priorities hinder longevity or permanence. It was emphasised that funding might well be prematurely withdrawn if signs of improvements appeared – or failed to appear – thus making long-term political commitment at risk from Pipeline Coordinators' successes and failures.

**Obstacles relating to Pipeline Coordinator Characteristics:** Discussions yielded views that Pipeline Coordinators might need to evolve to receive more permanent funding. For example, Pipeline Coordinators are currently primarily a form of 'push mechanism', being mostly concerned with selecting projects and providing grant-like funding, but there might be a need for them to become more of a 'pull mechanism' to make their work more needs-driven. Moreover, it was suggested that Pipeline Coordinators needed to have a global perspective and be more inclusive, as developers who are not supported by a Pipeline Coordinator are perceived by others in the industry as less attractive, leading to potentially greater difficulties in obtaining venture capital funding.

**Obstacles relating to Experimentation:** This related to the nature of the organisations being seen as experiments. In other words, they were seen as experimental ways of organising operations, and an important question is which type of governance is most efficient. This can only be found out by trying different kinds of Pipeline Coordinators before making any of them permanent.

## Recommendations

In order to deal with the identified obstacles related to the implementation of **Market Entry Rewards** and Milestone Prizes, and to making Pipeline Coordinators permanent, the following recommendations can be outlined:

- Regardless of type of incentive, **ensuring long-term financing is necessary**. That means

providing incentives with guaranteed financing over at least a decade, or even on a permanent basis.

- Regardless of type of incentive, they all need to secure **long-term political support at both national and transnational levels.**
- Regardless of type of incentive, they all need to be realized through **transnational collaborations and agreements.**

The common message from the participants was thus that it is not enough to identify specific incentives or to mobilise individual stakeholders. In order to get a significant amount of MERs, Milestone Prizes, and Pipeline Coordinators in place, there is a need for solution-oriented interaction among stakeholders at a transnational level. Thus, agreements have to be achieved among both public and private stakeholders, with different rationalities and financial strengths, implying that a number of conflicting interests have to be managed. However, the contemporary transnational engagement concerning development and supply of vaccine and diagnostics related to COVID-19 has shown this is indeed possible.

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