

## Report of the IMI consultation workshop on “Diagnostics for reducing antimicrobial resistance (AMR)” 19<sup>th</sup> June 2017, Brussels

### Background

In the past century, interventions and treatment with antibiotics have revolutionised our ability to combat infectious diseases. As a result, death rates from most infectious diseases have decreased considerably. However, because of their low unit cost for individuals (albeit high societal cost) and improved clinical outcome, antibiotics were overused which resulted in the pandemic spread of highly resistant bacterial clones. Because of the rising health threat associated with bacterial resistance, we need a paradigm shift in the way we deliver healthcare regarding infectious diseases: novel ways to prevent infections, innovative diagnostics and appropriate stewardship. Personalised medicine in infectious diseases, based on novel, rapid and reliable diagnostic strategies should help achieve this paradigm shift by identifying those patients who really need antibiotics, and by helping to select the narrow-spectrum antibiotic of choice.

The Innovative Medicines Initiative (IMI) initiated in 2012 a major programme called New Drugs for Bad Bugs (ND4BB) aiming at addressing the antimicrobial resistance challenge. Several projects address the resistance mechanisms, specialised clinical trials infrastructures, acceleration of development of new antibiotics and their combinations, and identifying new classes of products. A specific project, DRIVE-AB, aims at identifying new business models that balance conservation of antibiotics (rational use) and business conditions for continued investment into antibiotics.

With opening of IMI to the non-pharmaceutical sectors, the initiative and its ND4BB programme would be an ideal framework for joining forces between diagnostic companies, other private entities, public organisations and stakeholders to develop a vision on how diagnostics could help to ensure future generations are not faced with untreatable infections due to resistant bacteria.

There are five key ways in which diagnostics can help control the development and spread of global antimicrobial resistance:

1. Guide antibiotic treatment by identifying the patients who are likely to benefit from antibiotics and prescribing them only when necessary.
2. Identifying pathogen and resistance patterns: Rapid identification of the pathogen and its characteristics.
3. Monitoring resistance patterns: Surveillance of antimicrobial resistance patterns at all levels - national, local, hospital and ward level.
4. Surveillance: Tracking the spread of resistant pathogens by screening at-risk patients and healthcare workers for multidrug-resistant organisms.
5. Clinical trial optimisation: Supporting and facilitating clinical trials of new antibiotics by using diagnostics to enrich the trial population.

### Workshop objectives

- To consult with the relevant stakeholders on a potential Call for proposals under IMI2 addressing the topic ‘Diagnostics for reducing AMR’ that would aim at establishing a framework for value-based translation of innovative diagnostics into routine use to reduce AMR.
- To better understand the challenges and hurdles faced by diagnostic innovators for translation of early-stage products into validation, and value demonstration in primary and clinical healthcare practice.

- To obtain a better understanding of what evidence is needed from regulators, health technology assessment bodies and payers for implementation and adoption by healthcare systems.

## Setting the scene

The workshop opened by a video message from Pierre Meulien, Executive Director Innovative Medicines Initiative, highlighting the important role that diagnostics should play in addressing the antimicrobial resistance challenge. Angela Wittelsberger (IMI) then presented the IMI framework and basic principles as well as the objectives of this consultation workshop and the expectations from an IMI perspective.

Mark Miller (bioMérieux) presented the workshop goals and explained how diagnostics are being undervalued and underappreciated in AMR unlike therapeutics and vaccines and that this should change. The project currently envisaged by the diagnostics industry group committed to the project would not focus on technological aspects but rather on generating the research evidence needed to address the uptake and market penetration challenges of innovative diagnostics to address AMR.

The viewpoint of the World Health Organization (WHO) was presented by Francois Moussy, who made reference to the WHO global action plan where one work stream is dedicated to diagnostics for AMR. He stressed the critical role that diagnostics need to play to change the manner in which antibiotics are currently prescribed. He also presented the key role that the WHO has to play in raising awareness about AMR, better defining the needs of diagnostic tools, as well as contributing to development initiatives and facilitating their implementation in countries.

Timothy Jinks presented the perspective of the Wellcome Trust (WT): diagnostics for AMR need to be seen in the broader infectious disease context. Integration of diagnostics and therapeutics is key to address AMR challenges. The whole ecosystem must be effective for inventing, developing, AND most importantly implementation and uptake – deployment - of diagnostics.

It is critical to support the value of stewardship and the future IMI project should deliver trail blaze Dx development that would also have an impact in low and middle-income countries (LMICs). Implementation science is an aspect that the WT would like brought in.

Arjon Van Hengel of DG Research, European Commission (EC) summarised the relevant diagnostics projects currently funded by the European Commission, and the instruments that are in place for supporting diagnostics innovators such as the InnovFin Infectious Diseases instrument for loans jointly developed by the EC and the European Investment Bank.

We also heard that new diagnostics and new economic models and incentives are a key component of the new One-Health AMR Action Plan with its 3 strategic pillars whose adoption is foreseen for later this month. Arjon stressed the importance for pharmaceutical and diagnostic companies to have an intimate dialogue to tackle AMR challenges.

## Preliminary plans for a topic under the Innovative Medicines Initiative “Diagnostics in AMR”

Representatives from the diagnostics companies currently involved in preparing an IMI call topic presented their current thoughts of what the future IMI project should cover.

Volker Liebenberg (Thermo Fisher) presented the key success factors, tasks and deliverables for implementation. The outcome should be tested solutions for accelerating the approval and use of innovative diagnostics in AMR.

Gaps towards a standardised care network were presented by Philippe Cleuziat (bioMérieux) who stressed the fact that access to comprehensive micro-organisms and clinical samples is important. Sustainability will depend on the development of an organisational and network model allowing the extension/duplication to future studies related to infectious diseases.

Kieran Clarke (Alere) shared the group's thought on the design of a clinical study to demonstrate the value of diagnostics aiming at reducing inappropriate prescription and the spread of antimicrobial resistance. The objective of this clinical study would be to provide the evidence to support the uptake of available and new diagnostics in AMR.

During the discussion with the audience that followed, it was clarified that the reason of focusing on respiratory tract infections (RTI) was based on the available evidence showing that the majority of unnecessary antibiotic prescriptions were for this subset of infections, the significant size of this market, and that a choice needs to be made to select a test case, with results hopefully transferable to other indications. It was also clarified that the idea of establishing a clinical trial network in the "top 5 countries" in Europe still needs to be discussed in terms of selection criteria: high level of AMR, etc. The level of data sharing and the importance of involving payers should be clearly defined in the future topic text.

## Stakeholder perspectives and open discussion

After the presentation of the preliminary plans for a project under IMI, a round table was held to specifically discuss the value and challenges of diagnostics in clinical research. This was followed by a session where different stakeholders presented their views on

- the role diagnostics should play to address AMR
- the gaps and challenges that should be addressed by a potential call topic under IMI to support the value of diagnostics.

During the round table and the stakeholder's session, important input was given on how to further shape a potential IMI project.

Important messages received can be summarised as follows:

- The focus in diagnostics development the past years was on features of the new technologies rather than the benefit to the patient. The focus of a potential IMI project should be to address the implementation and uptake. To be successful, all relevant stakeholders through regulatory and approval should be engaged via a roundtable consultative approach, to ensure ownership by the relevant stakeholders. A key challenge remains reimbursement by payers; evidence of the benefits, of the outcome for patients is needed, and is what the project should be generating. In general, the point was made that it is important to understand who will be going to pay for the value that will be created.
- There is a common perception that patient management guidelines are not always followed by practitioners and that reference to IVD test (and use of) should be included in guidance, thus requiring further education on when to use IVD in order to manage AMR.
- From a regulatory viewpoint, it is important to address the new EU regulation in the project. Currently, standards and guidelines on evaluation methods for IVD evaluation are missing, as precision medicine is not commonly used in AMR. There is a need for precise diagnostics and well-designed clinical trials. A recommendation was made to actively approach regulators and seek guidance.
- From a health technology assessment perspective, the project should develop more pragmatic and simplified methods to assess the benefit and cost utility of diagnostics.
- SME's present at the workshop made the point that the role of SMEs was mainly to provide technology solutions. SME's challenge is to translate innovation to the market, this is a gap currently, and IMI should be the bridge that supports this translation and fills the gap.

- Several workshop participants called for including innovative technologies in the scope of the project. Others felt that investments made into novel technologies had not resulted in a big return, and that a project addressing the implementation challenge would then also incentivise new technology development. The term market access used to define the focus of the project was perhaps misleading; up-take, implementation would be more appropriate.
  - The current proposal of focusing on respiratory tract infections was challenged, and a few alternative ways were proposed for consideration by the group developing the IMI call topic. However, it was clear that the project will not be able to do everything, but that the intention is to rather start with a well-defined, smaller, and perhaps step-wise approach, and that it is expected that the results from the work focusing on one indication will be transferable to other indications.
  - From an academic perspective, it is important to develop clear guidance on what the target product profile of a new IVD should be, and what and when to measure. Algorithms for each type of disease and clinical guidelines are missing. A point was made that consideration should be given to the perception of AMR diagnostics by students.
  - From a clinical research perspective, it was stressed that a diagnostic test should be inexpensive, rapid with high sensitivity/specificity. The focus should be preventing both introduction and spread of bacteria into and within hospitals.
  - Databases and informatics tools should be stored from the start in a way that they can be shared easily later on; to ensure that data are collected in high quality and standardised way across as many countries as possible.
  - As the ideas around a potential project under IMI were preliminary and not fully worked out, it was noted by participants that certain aspects were not yet clear.

The scientific research agenda of the JPI AMR was suggested as a good source to tap into to support some of the details.

- Several workshop participants stressed that diagnostics companies should work more closely with pharma companies and vice-versa, that there is scope for collaboration, and were surprised by the lack of participants from pharma companies to the workshop (academia may help in respect to that bridging). Also, the collaboration between diagnostics companies and the treating physician should be strengthened. Diagnostics companies currently involved in the definition of a potential call topic have approached pharma companies and will continue to approach them.
- Several participants urged that the outputs of the project should be of relevance to the poorer countries, in Europe and in the rest of the world, and that the topic should be designed more explicitly in a way to ensure that the results will also have an impact on Low-Medium Income Countries (LMICs).

From a civil society point of view, diagnostics should play an integral, initial, continual and preventative role in addressing AMR in patients and animals. A strong message was put forward that industry should have LMICs in mind from the start since AMR is a global problem. The small market or low uptake in LMICs is often due to the fact that the wrong technologies for such environments are developed in the first place.

- It is important to define in what care setting diagnostics could best be deployed and shown to reduce antibiotic use. An important question that should be addressed was how to measure success of new diagnostics in reducing inappropriate use.
- It was further stressed that patient-centricity should be included as a concept, and that both patients and civil society should be included as important stakeholders.
- A sustainability proposition is important to include upfront in the project design. A potential project under IMI should tap into existing structures, and it is also expected that the outputs obtained from a project are transferable.

## Next steps

This workshop report will be shared with all participants and also published on the IMI website. The discussions and recommendations provided today will be taken into account when further developing a potential topic for a future call for proposals under IMI.

In addition, the group currently involved in the definition of a potential call topic under IMI will continue to engage with other companies and potential contributing partners, and is open to exploring synergies and complementarities with other initiatives.

Please join our LinkedIn group and regularly visit our website for news about this potential call topic.

## Annexes

- [Agenda](#)
- [Attendance list](#)