

## Identifying the pathway to diagnostic development

Report from the workshop on 1 May 2015

### 1. Background

The MRC and the JPIAMR are committed to coordinating and disseminating research into AMR. As part of this, we organised a joint workshop focussing on 'Identifying the Pathway to Diagnostic Development'. There have already been a number of global scientific meetings on this subject plus there are a number of on-going funding initiatives. Therefore, the focus of the workshop was how to bring this funding and research together to get potential new diagnostics into use, and to identify the challenges and opportunities along the way. The workshop was chaired Professor Herman Goossens and participating on the day were experts in diagnostics, from academia, industry, regulation, policy, and funding organisations.

We structured the workshop around three main sessions; Setting the Scene (human, animal, and industry settings), Identifying the Challenges and Potential Solutions Needed for Diagnostic Development, and the Funding Landscape. Each session had keynote speakers followed by a panel Q & A. We then identified four key areas to discuss in more detail in breakout sessions with feedback to the entire audience.

By identifying future challenges and opportunities in diagnostic development, the JPIAMR members aim to work together to find ways to address key issues and identify the next steps, for example, development of a road map for AMR diagnostic development.

### 2. Workshop discussions

The key note presentations covered a range of topics from the global need for diagnostics both in humans and animals, examples of how diagnostics have been developed for other infectious diseases, the regulatory landscape and the implementation of new technologies. There was also vigorous question and answer sessions during which the participants highlighted four themes where deeper discussion was needed but also where an EU wide solution could be envisaged. These were regulation, adoption, connections and resource sharing. There were a number of other themes of equal importance but time did not permit deeper discussion – in particular, diagnostics in developing countries and the economics of diagnostic.

#### Regulations

There have been some notable advances in the regulations around new antibiotics and the agencies are clearly engaged in helping deliver new diagnostics to market. There appeared to be a more consultative approach taken by the agencies both EU and US with clear willingness to develop the "science of regulation" with academic and industry partners. Academics/industrialists should engage with the regulatory agencies early in the development of a diagnostic. One issue that was considered a barrier was the divergence between the US and EU systems. The US system was considered to be more onerous but the potential market was much larger whereas the EU system allowed for more innovation but had a smaller market share. Any opportunity to converge on some issues should be explored.

Understanding and meeting regulatory demands could be difficult for academic and some smaller companies both in terms of administration but, more importantly, validation of new diagnostic tests. Diagnostic development would be helped by keeping within an "unregulated" environment

for longer to fully validate and to undertake "real world" evaluation. The UK is soon to launch a precision medicine catapult that will provide capacity to deliver this and there maybe opportunity to link existing centres across Europe.

Some thought also needs to be given to regulation of software and hardware as more app based approaches are developed. For example, would the smart phone on which the app is installed have to have regulatory approval? Some work has been conducted in the US with clear demarcation/differentiation between lifestyle and medical software but this is in its early stages and needs to be developed.

Potential role for the JPIAMR:

- Foster talks between US and EU regulators e.g. sponsored meeting
- Start to develop an EU wide network of diagnostic development centres e.g. building on infrastructures work, identify key centres, identify standards, capabilities etc.
- Develop better links between regulatory science and methodology development e.g. sandpits, workshop

### Adoption and implementation

It is becoming clear that there is a lot of advice available or becoming available to diagnostic developers on need, development, trialling and regulation but very few recommendations on how to get a diagnostic adopted into clinical or veterinary practice. With limited formal recommendations on the purchase of a test, it is unlikely that a company will invest heavily in its development. Increased and improved advocacy of diagnostic is needed to reassure purchasers that buying the test will improve outcomes. One way to do this may be to provide some funding for key centres across EU to provide evidence of real use of a diagnostic. If successful, the trial would act as an advocate for the adoption of a product. This would be after the clinical trial phase demonstrating safety and efficacy for regulatory approval. It would have to include a component of economic assessment and how the new diagnostic influences patient/animal care.

It was noted that purchasers are often absent from meetings of this type and so we may be missing a key voice in determining the direction of diagnostics research. The view point from purchasers may help provide clarity and transparency in how products are reimbursed. Diagnostics for bacterial infection are potentially unique in that the cost of the test may well be significantly more than the cost of the drug. Purchasers and suppliers will then need to work together with clinicians and vets to demonstrate how investing in such tests will benefit treatment and the full economic impact.

Potential role for JPIAMR:

- Encourage better engagement with purchasers
- Develop better mechanisms for advocacy across Europe

### Resources and sharing

The participants heard clear examples of how access to viral strains, clinical data and surveillance data underpinned the development of diagnostics for resistant HIV strains, an effect that was threatening the development of new antivirals. Clinical data and experimental data were shared between academics and drug companies and a number of clinical isolates and viral strains were collected, stored and shared. Not only did this lead to the development of new diagnostics but also provided a repository of samples to test new drugs.

It is clear that bacterial resistance and genotyping has added levels of complexity but it was highlighted that, at present, there were no fully accessible sample biobanks across the EU for clinical or veterinary bacterial samples. Some strains were commercially available but fresh clinical samples were very difficult to obtain due to availability but also the regulatory hurdles and having the correct ethical approvals in place.

As well as the samples, there needs to be more sharing of data sets generated from these samples. This should be at the level of the raw data rather than the interpreted experimental results. Much better data sharing platforms are needed to ensure better access but also to linkage with clinical, veterinary and environmental data. This is not unique to AMR and there

may already be solutions available that were not being used fully by the bacterial diagnostic community.

Finally, there should be a clearer view of the infrastructures available across the EU that can be accessed by diagnostic researchers. The JPIAMR is already undertaking such a review and the outputs should be communicated broadly.

Potential role for JPIAMR:

- Identify existing biobanks across EU and opportunities to network
- Develop a centralised biobank of samples that is fully accessible across the EU
- Sponsor specific working groups to establish how data can be better shared
- Sponsor specific working groups to determine what exactly is needed to be collected and how.
- Workshop or specific working groups "lessons learned in biobanking" from examples (good and not so good) such as UK Brain Banks Network <http://www.mrc.ac.uk/research/facilities/brain-banks/>, PHE example, any example of one that has set one up across the EU? etc.

### Connections

It was clear from all of the discussions on the day that key to accelerating development and use of new diagnostics was better communications between a very diverse set of stakeholders. This should start with early discussions between clinicians/veterinarians and the technologists to clearly identify parameters and limitations of a diagnostic test. However, this conversations should draw in, at as early a stage as possible, industrialists, fundamental research, regulators, end users, health care providers and patients to name a few. It was agreed that not all stakeholders need to be brought on board at the same time but conversations need to happen early enough in the gestation of a project to ensure that it can be shut down early if is not going to properly address the needs for which it is being developed.

The key question is how can these groups be brought together especially as funding streams involved work on very different timescales? Initiatives such as the Innovate UK Precision Medicine Catapult and the UK National Institute of Health Research Diagnostic Evidence Co-operatives provide core support for validation and evaluation and may provide a model to bridge the gap between academic funded research and company funded development. There should also be close coordination of academic/industry funding streams.

This type of collaborative research may be a new way of working for some researchers and often takes a shift in mindset to achieve. What is paramount is that all the groups involved understand the language – avoiding jargon and defining key terms. Collaborations of this nature also need active management with dedicated time.

Finally, collaborations must not be forced together in terms of people and indeed, in terms of science. The audience heard how diagnostics for animal infections were often using human biomarkers and break points as the underlying research in the animal realm was not available.

Potential role for the JPIAMR:

- Foster/sponsor multidisciplinary meetings on specific key issues, keeping them relatively small and focussed.