DEVELOP, EVALUATE AND IMPLEMENT

The role of laboratory professionals in developing and implementing tests was central to a recent clinical research symposium.

From biomarkers informing the rapid treatment of trauma and combating antimicrobial resistance, to blood tests diagnosing dementia or delivering personalised medicine, the clinical demand for *in vitro* diagnostics (IVDs) is ever expanding.

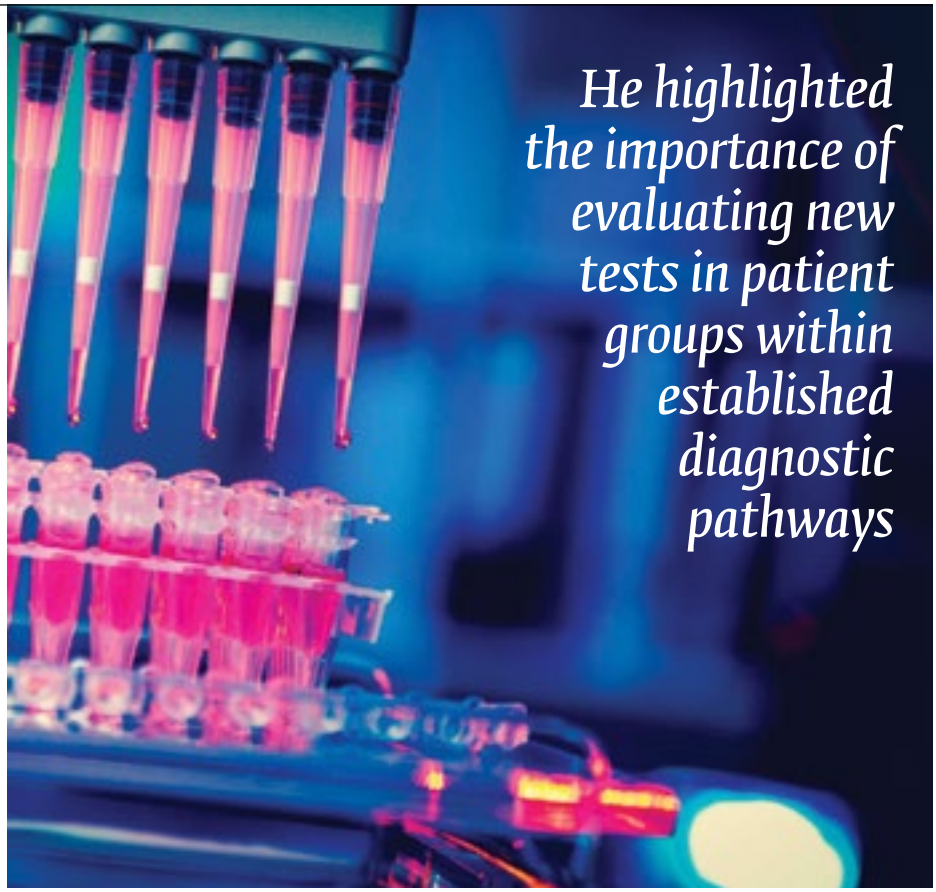
So, how do newly discovered biomarkers become new IVD tests in clinical practice? Balanced against demand is the necessity to ensure that IVDs are clinically appropriate, technically robust, economically affordable and, most importantly, evidence-based, which means research and development.

A lot has changed in NHS research over the last 10 years or so (for example, the National Institute for Health Research [NIHR] came in to being) and it is clear that there are a lot of organisations that contribute along the pathway, from invention to adoption and diffusion. To shed some light on this process, and on where NHS laboratory professionals might see the opportunity to contribute, the NIHR Clinical Research Network (CRN) West Midlands recently sponsored a symposium organised by the West Midlands Laboratory Medicine Research Group. Speakers were invited from some of the organisations involved to discuss their roles and open the door to ways in which they can, and do, work with NHS laboratory professionals.

The meeting brought together over 70 delegates from clinical laboratories across the UK and representatives from industry and academia to discuss IVD development pathways.

The speakers

The day was introduced with an overview from Dr Owen Driskell (CRN West



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Midlands Lead for Laboratory Medicine) which drew the landscape of test development and highlighted the lack of a recognised pathway for IVD development, compared to the established processes used to evaluate and implement new drugs and therapeutics. Dr Driskell discussed the potential roles for NHS laboratory professionals to contribute their expertise, stressing the need for collaborative working with clinical, academic and industry partners, a sentiment echoed by Professor Ramesh Arasaradnam, Consultant Gastroenterologist at University Hospitals Coventry and Warwickshire NHS Trust, who spoke about how he worked with his local laboratory to develop cut-off values for calprotectin.

Professor Jon Deeks continued the discussion, using cystatin-C and the enhanced liver fibrosis profile to illustrate the importance of capturing good data on biomarker biological variability and assay measurement error, and utilising these to inform study design and evaluation.

Professor Deeks works in biostatistics at the University of Birmingham and heads the Institute of Applied Health Research Test Evaluation Group, researching the development and application of novel tests. In a theme that continued throughout the day, he highlighted the importance of evaluating new tests in patient groups within established diagnostic pathways, together with evaluating performance against existing tests, something to which the clinical laboratory can contribute to significantly.

Clinical input

As new tests move from research to commercialisation, again, the input of clinical laboratories is valuable. Doris-Ann Williams, Chief Executive of the British In Vitro Diagnostics Association, discussed the industry need for access to patient samples for research and development, together with the advantages of beta testing sites to evaluate products at arm's length from the primary researchers. Over the last few decades the development of the IVD industry has been rapid, moving from early radioimmunoassay to the modern era of automation and sequencing. Doris-Ann explained how this expansion had been accompanied by a raft of regulatory change, including Good Manufacturing Practice, validation and tractability.

These regulations have recently increased further with the May 2017 publication of the new European In Vitro Diagnostic Regulation (IVDR), a replacement to the current IVD Directive, introduced in 1998. As Daryl Colombage, the Medicines and Healthcare products Regulatory Agency's Senior Medical Device Specialist, explained in a later talk, this new regulation is significantly different from the existing directive and strengthens current approval systems. The new regulation, which has a five-year transition period, provides for increased market surveillance and tractability, with a move to risk-based classifications.

Networks and innovation

Of note is the high failure rate in translating biomarker discovery into clinical practice. Successful adoption of a test requires both robust analytical performance and clinical effectiveness together with broader outcome improvements, and to demonstrate this an understanding of health economic and wider system impacts is vital. Carla Deakin, Associate Director of Market Access for the National Institute for Health and Care Excellence (NICE), discussed how NICE assesses the evidence for new technologies in the context of "value proposition", a comparative review of patient outcomes and health system priorities, and stressed the need to capture this evidence within the study design.

While this can be a complex, multifaceted issue, a range of support is available. Across England four NIHR Diagnostic Evidence Cooperatives (DECs) bring together a wide range of research methodologists, researchers, clinicians and patients to generate information on the clinical application and cost-effectiveness of IVDs.

Dr Mike Messenger, Deputy Director of Leeds NIHR DEC, illustrated the diagnostic accelerator pathway, again stressing the need to evidence wider service and economic benefit. Dr Messenger described examples of where

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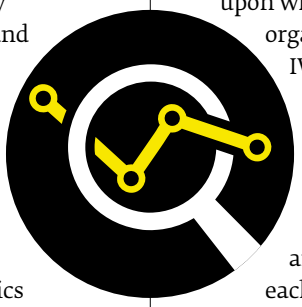
the DEC in Leeds is working with NHS laboratories, industry and academic partners in support of IVD development. Dr Phil Monaghan from the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) described an online tool kit that is being developed by the EFLM to support the assessment of unmet clinical need. Assistance is also available from the Clinical Research Network (CRN).

The CRN is part of the NIHR coordinated national network that enables and embeds high-quality research as core business across health and social care to make people and the NHS better. Sinead Collinge, Industry Operations Manager, and Ellen Edwards, Senior Research Support Facilitator, from the CRN West Midlands, described their roles in working with industry, academia and NHS professionals to support the design and delivery of NHS research, using the CRN Study Support Service.

Lucy Chatwin, Business Manager for the West Midlands Academic Health Science Network (AHSN), described the role of the AHSNs in providing a catalyst to generate adoption of innovations. Introduced in 2015, the mission of AHSNs is to lead and drive cooperation, collaboration and productivity between industry, academia and healthcare providers, and accelerate the adoption of proven innovation to generate health and wealth improvement. Within the West Midlands, a particular theme is the development of advanced diagnostics, genomics and precision medicine, and Lucy introduced Abdullah Sabyah from Rightangled Diagnostics with whom they had worked to develop and implement genomic diagnostic technology within cardiology.



Bringing the session right up to date, the formal presentations were concluded by Sean James, Genomics Ambassador for the West Midlands Genomic Medicine Centre, who gave an update on the 100,000 Genomes Project and its role in generating future diagnostic pathways.

Role of IVDs

Throughout the event, speakers reinforced the central role IVDs play in clinical pathways, and recurring themes included the placement of clinical need at the centre of development work, and the requirement to evaluate tests in appropriate patient pathways and groups with appropriate study design that captures informative outcomes and impacts. All the speakers stressed the importance of considering the requirements of the whole pathway, and not just the different stages, as evaluating the clinical need or the type of evidence required at an early stage dictates how you progress along any pathway and what support you might need.

In terms of the roles for NHS laboratories, there are possibilities at every stage along the pathway. Laboratory professionals' knowledge of current diagnostic practice within the NHS can inform the value proposition and the design and delivery of clinical trials and service evaluations. Discussion centred upon where the different organisations fitted along the IVD development pathway, with the Accelerated Access Review cited as a good place to start understanding the overview. The different organisations overlap in areas along the pathway, but each have different perspectives and functions with some being laboratory scientist led (the EFLM), others being NHS (the DECs, CRN and AHSN) or industry led (BIVDA) and others being non-departmental public bodies or regulators (NICE and the MHRA).

It was agreed that there are multiple needs and opportunities for NHS laboratory professionals to contribute their skills and expertise at multiple stages along this development pathway, with possibilities to collaborate and lead on future developments.

> *There are needs and opportunities for NHS lab professionals to contribute skills and expertise*

"From a laboratory perspective, we are generally presented with new tests to implement with little input into their design. By understanding the development pathway and collaborating with academic and industry partners, biomedical scientists and colleagues within laboratory medicine have the opportunity to highlight unmet need and to contribute to the development of new or improved laboratory tests" – Ian Davies, Academic Biomedical Scientist. BMS

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