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# The Role of Innovative Diagnostics in the NHS

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**In Vitro Diagnostics (IVDs) play a key role in healthcare management – the information from these tests can be used to diagnose or rule out causes of disease, to screen at risk individuals and to monitor response to therapy and manage diseases such as diabetes. IVDs are also essential to screen the blood supply in order to remove risk of infection during transfusions and play an increasing role in the prevention and prediction of disease.**

In vitro diagnostics, literally meaning "in glass", are tests performed on body fluids or tissue. Most tests are traditionally performed in hospital pathology laboratories and in public health laboratories. With miniaturisation of technology and simplification of procedures, an increasing amount of testing is now done in a point of care setting either within a hospital but also closer to the patient such as on a ward or in Accident & Emergency. This also includes in the community by GPs and other healthcare professionals, or by individuals themselves, including self-monitoring of blood glucose levels by people with diabetes. Simple products like pregnancy kits, bought over the counter, are IVDs.

There are many emerging health needs which IVDs can address including antimicrobial resistance, helping with unmet clinical needs and saving NHS resources within patient pathways. Three separate examples illustrate the role which IVDs can play to improve healthcare.

The first is the use of diagnostics to identify patient cohorts who might respond to specific drug therapies. These have been known as companion diagnostics but could also be termed Diagnostics Dependent Drugs – as without the test, the drug should not be used. There is a rapidly increasing number of these and to date they have mostly been in the area of oncology. Their use will be supported later in 2015 when the Government funded Precision Medicine Catapult will open with the role of supporting the use of diagnostics to enable more tailored treatments, "precision medicine".

Pharmacogenetics is the response of an individual to a specific drug according to their genetic profile. In precision medicine, tests can be pharmacogenetic or they can be used to identify other factors such as a protein produced by certain cancers as in tumours producing the protein HER2neu responding to Herceptin in breast cancer. These drugs are expensive and highly toxic so it is beneficial both to the NHS and to the patient not to use drugs which won't work.

*"The upcoming years may well be known as the age of diagnostics"*

*Janet Woodcock, Director of CDER, FDA April 2012*

In February 2012 vemurafenib (Zelboraf, Roche), an inhibitor of BRAF kinase, was approved by the European Medicine Agency for the treatment of patients with unresectable or metastatic melanoma with the *BRAF* V600 mutations. Vemurafenib produced improved rates of overall and progression-free survival in patients with previously untreated melanoma with the activating *BRAF* V600 mutation compared with standard first-line treatment with dacarbazine. Reliable detection of *BRAF* V600 mutation is therefore critical for therapeutic choice in these patients and a companion diagnostics test (the cobas 4800 *BRAF* V600 mutation test produced by Roche Molecular Systems) has been developed and validated. The cobas 4800 *BRAF* V600 mutation test has been validated in national and international collaboration studies. It allows the treatment of vemurafenib providing that:

- the patient has been diagnosed with unresectable or metastatic melanoma
- *BRAF* V600 mutation analysis test is required for diagnostic purposes to guide therapeutic decision-making.

Routine tests used in hospital laboratories are now numerous across disciplines such as biochemistry, haematology, microbiology, histopathology and immunology. The role they play can be as simple as providing a small amount of information to add to the whole clinical picture of the patient, in the same way as knowing blood pressure and temperature. Increasingly tests are being developed to play major roles in specific disease pathways. One area of clinical need for better and faster tests is in Sepsis – for every hour this serious infection is undiagnosed and treated, the mortality rate increases by 8%. Improving precision of diagnosis will assist in the battle against antimicrobial resistance too. It will allow rapid

targeted use of the right antibiotic rather than using a broad spectrum antibiotic. Cultures can be made to identify pathogens in the traditional way microscopically, but this can take several days – time which these patients may not have. A major global IVD provider, Abbott Laboratories, has developed a system which couples PCR technology to mass spectrometry to allow identification of pathogens and actionable results from a 5ml blood sample within six hours. This system, Iridica, has been available to the NHS from March 2015.

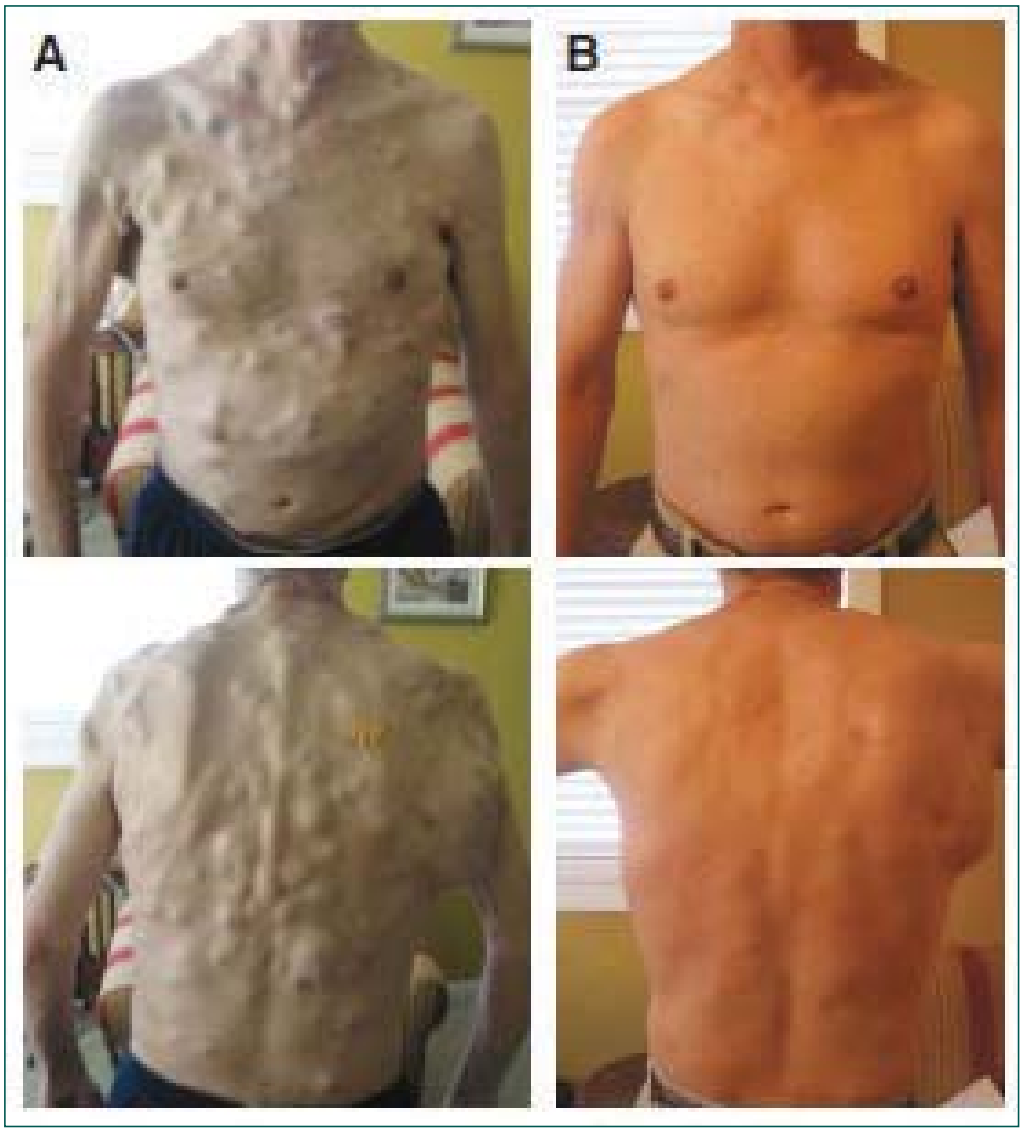
This winter, the NHS Accident & Emergency departments were under huge pressure and hospital beds were full. Point of Care tests in the community can help reduce unnecessary admissions by allowing people, particularly those with multiple chronic conditions, to be helped in the community. In Abingdon, Oxfordshire, Dr Dan Lasserson, a primary care clinician with extraordinary energy, has developed a successful model of care over the past four years. Either paramedics or GPs can refer unwell people to his Emergency Multidisciplinary Unit (EMU).

Within a mean of 61 minutes from receiving the call, a patient will have been examined and had point of care testing performed allowing a rapid and accurate diagnosis. Many can be treated and sent home. Data show this service is reducing hospital admissions from these patients by 85%. Where patients do need hospitalisation, they can be sent directly to the appropriate ward, allowing treatment to begin more quickly than if they had been admitted straight from the community.

As well as saving hospital bed use this centre is seeing much better outcome for what are often frail and elderly people. In 2011/12 the savings to the NHS from the Unit were £1.9 million (source: Oxford University Dept. of Primary Care). The Abingdon EMU has proved so successful that a second EMU has been opened in Witney with two further Units planned in Banbury and Oxford itself.

*"Hospitals are dangerous places, and it is vital to avoid unnecessary admissions and develop better services for older people in the community and in their own homes"*

*The King's Fund, March 2012*




The pictures show the benefit of identifying a patient which can be treated with the right drug. This 38-year-old man had *BRAF* mutant melanoma and miliary, subcutaneous metastatic deposits. Photographs were taken (A) before initiation of vemurafenib, and (B) after 15 weeks of therapy.

These three examples are just a few of the ways that diagnostic tests underpin healthcare. They create wealth for the economy. The IVD industry sector employs more than 8,000 people in the UK with exports contributing more than any other medical technology sector – £1 billion annually and increasing. Better use of IVDs also benefits society as they reduce time lost in attending hospital appointments and enable people to return to fulltime employment more quickly.


Some of the simple point-of-care equipment which allows rapid testing of patients in a community setting.

# THE FUTURE OF LIFE SCIENCES IN THE UK

Dr Malcolm Skingle CBE
Director, Academic Liaison,
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**The UK science base attracts more than its fair share of Pharmaceutical R&D funding. If you consider the UK Pharma R&D spend as a proportion of the total Global Pharmaceutical R&D spend it equates to 9% and yet the UK percentage share of the world prescription market is just around 2% of the market. The UK Life Sciences sector is already punching well above its weight, underpinned by a strong academic science base. In the coming years, as the science bases in other countries gain ground, Government and industry must work together in partnership to ensure that UK science base remains strong.**

The pharmaceutical sector has experienced well-documented pressures, one of which is the cost of medicines, especially as the ageing population increases. Governments want to reduce healthcare costs. The USA currently has a little over a third of the world's prescription sales and yet it only has 4.4% of the world's population. The Americans are currently spending a little under 18% of GDP on healthcare (the figure for the UK is 9.4%). Further rising healthcare costs are not sustainable.

China and India have a combined population of more than 2.5 billion people. As their economies get stronger their respective populations are demanding better healthcare treatments. We are already moving beyond communicable diseases in places like Africa, as more control is taken of infection, and attention is turning to non-communicable disease such as diabetes, cardiovascular disease and cancer. The pharma industry will need to collaborate and work with these developing science bases to be able to run effective clinical trials, and to help patients.

*... The pharma industry will need to collaborate ...*

## PREVENTION VS CURE

Encouragingly, Life Science research in the non-communicable diseases will increasingly focus on prevention rather than cure. For example, fitness and dietary considerations will be taken into account whereby governments will work with food manufacturers to address the obesity epidemic caused in part by the amount of sugar in food and drink.

Vaccines will become increasingly important in combating global disease. Many diseases have been eradicated from parts of the world following extensive vaccination programmes. Diphtheria, polio and smallpox have been eradicated and the incidence of other killer diseases dramatically decreased. We still face challenges in the developing world and it has been calculated that 22 million children are without access to vaccines. Around 19,000 children under the age of 5 die every day from largely preventable diseases.

Vaccines represent 2-3% of the total Pharma sales but this market has rapidly expanded from a $5 billion market in 2000 to $24 billion in 2013. The WHO estimate that it will be $100 billion by 2025. The UK is well placed to undertake much of this pioneering research. GSK currently produces more than 25% of the

world vaccines; around 2 million doses every day and distributing to 170 countries. It has 16 vaccines in development including an Ebola vaccine in clinical trial.

## MONITORING HEALTH

The continuum from wellness to illness will be better tracked through careful pheno & genotyping as individuals take greater responsibility for their own healthcare. Health status, in the future, will be monitored using electronic technologies, allowing us to track our health status using sophisticated Apps to measure physiological parameters and level of fitness. We already have heart rate monitors and pedometers on our mobile phones; these Apps will become more commonplace and will be used to measure routinely a range physiological parameters including blood pressure, body fat, forced expiratory volume, blood glucose and pO2. Ultimately individuals will have their electronic health records, genetic profile and current physiological parameters on a portable device, possibly a wristband or smart watch. This will enable clinicians to make a more rapid and accurate diagnosis when a patient attends the clinic or indeed is assessed from a remote location.

## CONVERGENCE

There will be further convergence of technologies in healthcare. We are already using, in certain disease states, diagnostic technology to define more precisely patient populations in clinical trials and post-approval to ensure that the patient gets the right drug at the right time. In parallel we are also exploring how the body can respond to electrical impulses in real time in order to bring about a local physiological response. The term electroceuticals has been coined for this evolving area of science and we have an active programme where we are collaborating with several academic groups.

All of the above healthcare innovations will require research from multi disciplinary teams and we are well placed in the UK to lead much of this research. Pharmaceutical R&D investment accounts for 22% of the total industrial R&D in the UK; which is more than any other sector and indeed the next two nearest sectors, automotive (11%) and ICT (10%), put together.

*... GSK currently produces more than 25% of the world vaccines ...*

## AN AGEING POPULATION

With improved sanitation and the use of antibiotics and cardiovascular drugs people are living longer. As a result we are seeing an increased incidence of chronic degenerative diseases associated with ageing eg dementia and cancer. Medicine has advanced dramatically over the last 100 years and we have seen several waves of new therapeutic innovations resulting in a step change in how we practise medicine. For example, the cost of gene sequencing has come down dramatically since the human genome was first sequenced and reported back in 2001. With new technology, some developed here in the UK, it is now quicker and cheaper to genotype individuals and this is allowing us to stratify patient diseases in a way which has not previously been possible. GSK have recently set up a collaboration with the European Bioinformatics Institute and the Sanger Centre at Hinxton to systematically mine biological data. We intend to tap into the expertise in these centres and combine it with our own to use the large data sets that are publicly available to help us validate therapeutic targets. It is our belief that using genomics and proteomics to identify drugs against targets identified from disease genes will yield novel medicines. Advances in genetics have helped us to identify and monitor several diseases which were previously very poorly treated.

*... individuals will have their electronic health records ...*

*... The term electroceuticals has been coined ...*

*... using genomics and proteomics to identify drugs ...*

The pharmaceutical industry has made some significant health advances over the last 20 years. For example HIV/AIDS has been transformed from a death sentence to a chronic condition with the new therapies. This has resulted in an 80% reduction in death rates over this period. Similarly new therapies to treat cancer have contributed to a 20% decline in cancer deaths such that today, 2 out of 3 people diagnosed with cancer will survive at least 5 years.

New treatments have also been developed for multiple sclerosis and rheumatoid arthritis; and rather than focusing on the symptoms of the disease, as was previously the case, we are now focusing on the underlying aetiology of the disease in order to slow progression and drive patients into remission.

The net effect of several factors spanning health and welfare is that we are keeping people alive for longer at a time when the world population is expanding. The population has grown almost 4 billion since I was born. The current world population is 7.3 billion with a forecast of 9.1 billion by 2050. From a pharmaceutical company perspective this represents both a threat and an opportunity. Only by working with our academic collaborators and "fleet of foot" biotech companies will the pharmaceutical industry be able to innovate to develop desperately needed new medicines. With the continued support of the UK government, the UK academic base is ideally placed to underpin a vibrant life sciences industry in the UK.

**Professor Guy Poppy**, Chief Scientific Adviser, Food Standards Agency, also spoke at the meeting. A summary of his talk will appear in the next issue.