

For personal use only. Not to be reproduced without permission of the editor  
(permissions@pharmj.org.uk)

# The impact of new technologies on hospital pharmacy

Aspects of quality and safety introduced by new therapies, including genome technology, were discussed at the 12th EAHP congress. Hannah Pike reports

**P**harmacists can play a role in moving the application of pharmacogenetics from the laboratory to the patient's bedside, said William Evans, St Jude Children's Research Hospital, Memphis, Tennessee, during his keynote presentation.

Dr Evans explained that the technology behind pharmacogenetics is currently much further ahead than the science (such as the pharmacology and the genetics), and there is still a lot of work to be done to establish robust diagnostic models. However, progress is being made, for example in the use of pharmacogenetics in the research and treatment of diseases such as leukaemia.

Genetics can have an overwhelming influence on the action of drugs, said Dr Evans. He described the work of his team in using the technology to elucidate the genetic determinants of drug response to treatment for acute lymphoblastic leukaemia.

Pharmacogenetics will enable us to divide patients into sub-populations based on their ability or inability to respond to a drug, or their predisposition to drug toxicity, he explained, rather than grouping patients into "textbook" categories.

"If you genotype a patient correctly you only have to do it once, unlike blood sugar or serum creatinine," he said. If that information is put into a secure database, the patient

could authorise their pharmacist or doctor to access that information, which could aid clinical decisions about drugs known to be affected by genetic make-up.

Dr Evans added that there has been some scepticism from the medical profession about the use of this technology. For example, doctors who have been prescribing a drug for years may find it hard to understand why a genetic test is suddenly needed.

"Regardless of whether you are working in cancer, cardiology or other areas of health care, genetics and genomics are ultimately going to impact the way you treat patients and make decisions about drug treatment and drug doses," he said.

## More guidelines needed for safer clinical trials

Using flexible testing strategies and applying a precautionary principle to clinical trials might have avoided last year's incident in the testing of the monoclonal antibody TGN1412 at Northwick Park Hospital, said Nirmala Bhogal, from the Fund for the Replacement of Animals in Medical Experiments, Nottingham.

She said that additional guidelines specifically covering the clinical testing of biotechnology products are needed (there are currently four or five documents available worldwide).

"We have novel biotherapeutic [agents] being developed at a dramatic rate. Some of them have modes of action that resemble products that are already marketed, but many do not," Dr Bhogal said. She explained that where a mechanism of action is very different from a known mechanism or a drug is likely to cause multiple effects then caution is needed in clinical studies. Such drugs should be tested on a single volunteer and administration should be staggered.



Nirmala Bhogal: access to prior information is important

During animal trials of TGN1412, macaques developed some (mild) adverse effects two hours after being given the drug. The volunteers should have been given the drug no sooner than two hours after each other, she said, but it was administered to them within minutes of each other.

Turning to the need for information, Dr Bhogal said it is important to have access to as much information as possible that has previously been collected about the drug. There

is evidence that TGN1412 was not the first antibody to cause cytokine release. "Why isn't this information in the public domain?" she asked.

It can be difficult searching the literature for information about drug pathways or processes because the information is often presented in different formats and not presented statistically. "Comparison meta-analysis data is absolutely dreadful at the moment," she added. Another obstacle is obtaining the required data from pharmaceutical companies.

Various testing schemes have been proposed for clinical trials but we need better schemes for pre-clinical trials, she said. In the case of TGN1412, none of the preclinical studies was able to predict the effects seen in the human volunteers.

These studies will potentially take years to conduct which will be unpopular with the regulators and pharmaceutical companies, Dr Bhogal said, but we do not currently have simple, fast screens for bioaccumulation and immunogenicity.

Dr Bhogal said that clinical trials need to be designed on a case-by-case basis. "Guidelines are guidelines. It is down to individual pharmaceutical companies and clinicians to ensure that how they test the product is the best for that particular product," she said.

The 12th congress of the European Association of Hospital Pharmacists, entitled "New therapies in the 21st century: challenges for hospital pharmacy", was held in Bordeaux, France on 21–23 March. **Hannah Pike** is editor of *Hospital Pharmacist*

# Challenges of unlicensed drugs in Europe

**Purchase of unlicensed oncology medicines** is now routine in the pharmacy departments of tertiary care hospitals across Germany, said Irene Krämer, director of the pharmacy department, Johannes Gutenberg University Hospital, Mainz. Speaking at a satellite symposium sponsored by IDIS, professor Krämer said that oncology drugs are the most common and the most expensive imported drugs in Germany.

She explained that legislative changes have meant that a number of drugs formerly licensed in Germany now need to be re-approved, and many drug companies are not willing to go through this procedure with drugs that have a small share of the market. Since most of these drugs have been used for decades as part of internationally approved protocols, they are not considered to pose a risk, despite their unlicensed status.

Professor Krämer outlined the restrictions on purchasing unlicensed drugs and explained that, under German legislation, imported drugs may not be stocked in the pharmacy. Furthermore, the pharmacist is personally responsible and liable for the quality and safety of drugs imported.

Professor Krämer said that there is still a problem with reimbursement for unlicensed drugs in Germany, and obstacles to overcome regarding the compassionate use of these drugs.



Irene Krämer: the pharmacist is personally responsible for the quality of imported drugs

## — Risk assessment

Allan Karr, pharmacy business services manager at University College London Hospitals NHS Trust gave the symposium an overview of the role of hospital pharmacists in dealing with unlicensed medicines in the UK, including their roles in drug and therapeutics committees, quality assurance, clinical pharmacy, purchasing and the dispensing service.

Mr Karr also said that although risk assessments are now commonly carried out, he does not believe that enough attention is focused on risk reduction. Risk reduction areas include:

- Assessing the clinical risk. Is it worth using an unlicensed medicine for a self-healing skin condition, for example?
- Quality assurance. Is the expense of analysing a product in a full quality assurance assessment warranted?
- Ensuring that patient information is translated into English.
- Promoting reporting of adverse drug events to the Medicines and Healthcare products Regulatory Agency.
- Providing GPs with full details of the unlicensed product.
- Keeping full records, including details of any adverse reactions and records of any risk assessment and risk reduction tools.

Mr Karr said that at UCLH they are currently developing a software application, together with Guy's and St Thomas' NHS Foundation Trust, to standardise a risk assessment and risk reduction tool.

"We hope that in the next year or two we will have an application that will help improve the way we manage unlicensed medicines and reduce risks," he said.

# Shortages of medicines in the European Union

**Hospital staff** need more and better information about changes in drug preparations to deal effectively with the problem of drug shortages, said Walter Deutschmann, from Klinikum Bremen Mitte in Germany.

He said that his hospital pharmacy supplies drugs to four hospitals, with a total of about 3,600 beds. They conducted a four-year study into the effect of drug shortages and bottlenecks (defined as a manufacturer not being able to deliver a drug within one week) on the hospital.

Results showed that there was an average of 100 bottlenecks per year, with the incidence of supply problems increasing each year. Dr Deutschmann said that the staff were rarely informed by the companies about stock problems. "Mostly, we had to ask for outstanding deliveries or were informed merely by the shipping papers of other products," he said.

The shortages were overcome by using existing stock or another pack size (in 56.7 per cent of cases) or procuring an identical preparation from a wholesaler (in 11.9 per cent of cases). In 28.7 per cent of cases the

patient was given a different drug, either imported (4.2 per cent of cases), an identical preparation from an alternative manufacturer (21.7 per cent of cases) or a different drug with a similar mode of action (2.8 per cent). In 2.6 per cent of cases it was not possible to make a suitable substitute.

Dr Deutschmann explained that, with the exception of some antidotes, German legislation does not allow unlicensed drugs to be stocked in pharmacies. The unacceptable delay in getting a drug to a patient that would occur if the drugs were procured in the usual way means that hospital pharmacies do stock imported drugs, but are in conflict with the law.

Dr Deutschmann said that about 840 working hours were spent managing the drug shortages over the four year study period. In addition to being time consuming, the market price is also affected. "In 2006 supply bottlenecks resulting from the shutdowns of intravenous immunoglobulin preparations and other blood derivatives led to subsequent rationing and a considerable increase in prices," he added.

## — Regulatory changes

Rui dos Santos Ivo, from the European Commission, said that there is clearly a need for regulatory changes to support the availability of medicines across Europe. He gave an overview of recent reforms to pharmaceutical legislation covering issues such as the obligation of continuous supply by wholesalers, the organisation of data protection periods, measures to reinforce pharmacovigilance and new rules on labelling and patient information leaflets. He acknowledged the challenges involved in translating these directives into practice.

He summarised ongoing and future European initiatives to support medicines availability. These include changes in legislation regarding studying drugs for paediatric use, and the creation of a European database containing information on all medicinal products for human or veterinary use that have been authorised in the European Union and the European Economic Area. The database, currently under development, can be viewed at [www.eudrapharm.eu](http://www.eudrapharm.eu).