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Cover photo: Pills with different hues (see *The Power of Drug Colour* on page 13).



A year of challenges, a year of work

Time flies! It seems only yesterday that we were in Sofia listening to our guest speakers, and here we are already – at the moment in time when I have the great pleasure in looking forward with anticipation to seeing you all once again soon in Edinburgh for our General Assembly on the 18–19 April. Immense thanks go to the Royal Pharmaceutical Society, and particularly to Janet Halliday, for offering to be our distinguished hosts this year, and also for organising the Scientific Symposium on Friday 17 April at the University of Strathclyde on Advances in Technology Impacting the Pharmaceutical Industry.

Yes, it has been a year of challenges, to continue to target the objectives I committed myself to when you gave me the honour of accepting me as your President in Brussels. PHAR-IN, the emergence of biotechnology, participation in the European Medicines Agency Interested Parties forum, continuing to address medicines shortages, responsible transparency, the update to Annex 16 – all these we have worked on, as you will see when we meet at the General Assembly, and I must offer my heartfelt thanks to my colleagues on the Bureau and to others in the EIPG who have contributed tirelessly and selflessly to this hive of activity.

In particular, I would like to highlight the webinar recently organised conjointly between the European Pharmaceutical Students' Association and the EIPG at which Claude Farrugia and Georgina Gal delivered well-received presentations



– so well received, in fact, that an “encore” was requested and duly organised. It represents but a fraction of the renewed impetus with which collaboration between these two organisations has been rediscovered over the past year, thanks to the energy and drive of our Vice President for Education and Careers, Anni Svala. This aspect of the EIPG activities is a key “raison d’être” of EIPG, for our commitment to industrial pharmacists is not limited to today’s

professionals, but also, importantly, to those of years to come. It is with this principle in mind that EIPG continues to give due importance to interaction with budding industrial pharmacists at its General Assembly and pre-assembly Scientific Symposium.

Yes! A year of challenges and a year of work, and never a moment to rest on our laurels, as we prepare to proudly participate as an observer to the US Pharmacopeia Convention in April 2015 in Washington. “Mais pas plus pour l’instant”. There will be time for that, and more, when we meet soon.

Welcome to Edinburgh!

A handwritten signature in black ink, which appears to read "Paccioni". The signature is stylized and fluid.

Jean Pierre Paccioni
EIPG President

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INTERNATIONAL EFFORTS TO PROTECT PATIENTS FROM UNSAFE PHARMACEUTICALS

by Jim Dahl, Thomas T. Kubic and Marv Shepherd

The public and private sector, law enforcement and government have worked to build relationships, strengthen regulation and improve product packaging to protect patients across the world from unsafe medicines that are trafficked by transnational criminal organisations. Our efforts have had a significant impact, but the problem remains.

Jim Dahl is a subject matter expert in pharmaceutical crime and malicious product tampering with over 30 years of US federal law enforcement experience. Dahl served for 9 years as Assistant Director of the US Food and Drug Administration's Office of Criminal Investigation and in private industry as Global Product Security Director at Eisai Company Ltd., as the principal of his own independent consulting company and as Senior Managing Director for Crisis Management at an international security consulting firm.

Thomas T. Kubic is President and CEO of the Pharmaceutical Security Institute (PSI), a non-profit association dedicated to protecting the public health by sharing information and initiating investigations into unsafe medicines by the authorities. A former executive with the FBI, he now represents the PSI at numerous international meetings, conferences and seminars. The PSI's collaborations include working with international and national level authorities, including INTERPOL, the United Nations Office on Drugs and Crime and the World Customs Organization. He is an officer with the Partnership for Safe Medicines, and serves as an advisor to the Permanent Forum on International Pharmaceutical Crime and INTERPOL's Pharmaceutical Industry Initiative to Combat Crime.

Dr. Marv Shepherd is Director of the Center for Pharmacoeconomic Studies and Chairman of the Center for Pharmacoeconomic Studies College of Pharmacy University of Texas at Austin. Dr. Shepherd examines policies related to drug importation and re-importation (especially from Mexico), the use of drug anti-counterfeiting strategies and techniques for monitoring prescription drug diversion. His research and expertise on drug importation and counterfeiting has been featured in major media outlets in the US. He also serves as President of the Partnership for Safe Medicines.

The situation in 2013

The Pharmaceutical Security Institute, which has collected data on counterfeiting, illegal diversion and theft incidents for twelve consecutive years, reported a rise in counterfeit drug incidents and illegal diversion incidents in 2013. The 2193 incidents of pharmaceutical crime which were reported were a significant 8.7% increase over 2012 – the highest annual total ever documented. Among those incidents were 406 illegal diversion cases, a 24% increase over 2012 (see Figure 1).

Reporting also showed changes in which medicines were being sold and how they were shipped.

Counterfeiters narrowed their product lines from 523 different



Figure 1: Diverted drugs. (Photograph courtesy of the US Federal Bureau of Investigation).

medications in 2012 to 317 in 2013. They also moved back towards sending their products in larger shipments. Of 1156 counterfeiting incidents involving medicines obtained in either customs seizures or police/health inspector raids, 526 (46%) counterfeit medicine seizures were "commercial" size. In 2012, only 40% of the 841 seizures were of a commercial size.

Finally, there was an uptick in enforcement. Arrests of people involved in the counterfeiting, illegal diversion and major thefts of pharmaceuticals increased 18% to 1460 this year. Arrests of those engaged in illegal manufacturing increased 151%, reversing a 3-year downward trend. Sixty-three illegal pharmaceutical manufacturing facilities (IPMFs) were detected in 2013, an increase from 37 IPMFs found last year. There were 426 incidents where counterfeit products reached licensed wholesale distributors and/or pharmacies in 49 different countries. This was a decrease of 12% from 2012 (see Figure 2).

International cross-agency efforts

Solving the counterfeit problem relies fundamentally on international cross-agency efforts, and, in recent years, we have strengthened communication and coordination across the entire pharmaceutical supply chain.

Enforcement agencies combined efforts to combat illegal medicines in over 40 nations. According to published reports, they made 2636

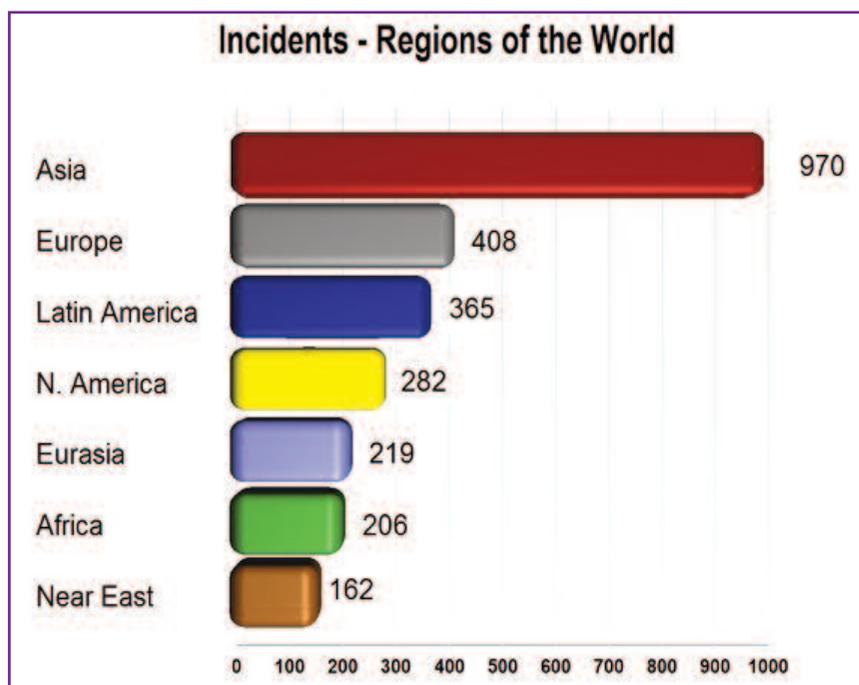


Figure 2: Counterfeit drug incidents worldwide, by region, 2014. (Courtesy of the Pharmaceutical Security Institute).

arrests on a global basis and seized more than \$757,000,000 in illegal medicines. In May 2014, INTERPOL coordinated Operation Pangea VI, an international action week against illegal online sales of medicines during which 198 agencies seized 9.8 million doses of medicines in 113 countries and shut down 11,800 websites. The World Customs Organization's (WCO's) Operation BIYELA 2 intercepted more than 113 million illicit, counterfeit and potentially dangerous pharmaceutical products at 15 African ports.

Non-governmental organisations (NGOs) and the public sector have been active. Eight African nations took steps ranging from joint operations with the police and customs services to outright bans on the importation and sales of medicines from certain countries. The International Federation of Pharmaceutical Manufacturers and Associations was joined by ten major NGOs in a new program, 'Fight the Fakes,' which was designed to raise consumer awareness, a challenge identified by the WCO. Pharmacist associations reiterated the messages of drug regulators concerning the problem

of herbal medicines that contain active pharmaceutical ingredients, which, in the case of Nigeria, resulted in further complications in the medical conditions of patients.

More private companies have also joined the effort. In February, Baidu signed a partnership agreement with China's Food and Drug Administration to promote the safe acquisition of medicines over the internet by providing credible drug information online and shutting down sites that disseminate false information. Teva, a generic medicines manufacturer, publicly reported working with the authorities to disrupt a criminal organisation working in four European countries^{1,2}.

Legal reforms

Significant progress in improving legal structures and regulations has been seen in 2013 and 2014 to better prevent and prosecute counterfeit pharmaceutical crime.

The Council of Europe's Medicrime Convention, which establishes a standard to prosecute counterfeit medical products on a public health basis, is gaining momentum. At present, 20 European states, as well as Guinea,

Israel and Morocco, have signed the Convention. It has been ratified by four Council of Europe member states – Hungary, Spain, Ukraine and Moldova – and will take effect once five member states have ratified it.

The Convention creates a legal framework that makes the manufacture and sale of counterfeit medicines and similar crimes illegal in and of themselves and a separate offense from any intellectual property violation. It harmonises definitions of criminal activity impacting public health, promotes cooperation and prevention/awareness activities between parties, and criminalises other activities often found hand-in-hand with counterfeit drugs. These include offering to or attempting to supply illegal product; falsification of a broad range of documents used in these offenses; possession of products, materials, accessories or falsified documents with intent to commit criminal acts; and intentionally placing products on the market without authorisation. It covers medical devices in a similar fashion³.

In addition to the Medicrime Convention, several countries have made strides to improve their regulation of the drug supply chain. The US Drug Supply Chain Security Act, which was signed in November 2013, creates a national standard that supersedes fragmented state legislation by codifying the responsibilities of supply chain actors to verify the licensing of their trading partners, label and track pharmaceuticals, investigate suspicious products, and share information. In December 2013, Brazil passed a track and trace law which provides for unit-level serialisation and tracking throughout the entire drug supply chain^{4,5}.

The European Union Directive 2011/62/EU requires serialisation of all salable products followed by authentication of the serial number at point of sale. The Directive introduced as a general rule that medicinal products subject to prescription should bear the safety features unless an assessment shows

the absence or limited risk of falsification, i.e. affixed safety features on outer packaging⁶.

Several countries have increased penalties for drug counterfeiters. In July 2014, Russia amended its criminal code to raise the maximum penalties for the production of counterfeit medication to 5 million roubles (\$150,000) and up to 12 years in prison. Kenya and Ecuador have also passed reforms⁷.

Cross-agency/country cooperation

The US Food and Drug Administration (FDA) has extended its international efforts to improve enforcement. In 2014, for the first time, an agent from the FDA's Office of Criminal Investigations (OCI) will be assigned to Europol to more effectively carry out international investigations. The FDA continues to work with INTERPOL on investigations and projects such as Operation Pangea VI⁸⁻¹⁰.

Fighting counterfeit drugs with packaging

Pharmaceutical companies are improving drug packaging to resist the efforts of counterfeiters. The FDA has recommended that pharmaceutical manufacturers protect their products by using a multiple, periodically changing, layered approach with at least one covert marker. Many companies today have responded by employing three or more overt and covert markers on drug packaging and some companies employ product forensic markers.

Overt markers

Overt markers on drug packaging are visible to the naked eye. Common overt methods include holograms, colour-shifting inks, watermarks and raised printing. Some of these may appear on the product packing; others on product package inserts. Holograms are widely used by many industries, not just for pharmaceuticals. Today holograms can be very sophisticated and some even have covert markers inside the hologram,

along with embedded serial numbers. Polychromatic inks, which change colour depending on the angle from which they are seen, are commonly used as an authenticity marker for many industries. Many nations, including the US, use colour-changing inks on paper money and this approach is a common authenticity approach for pharmaceutical products. For example, Pfizer uses colour-shifting ink on Viagra® packaging. Another overt technique is the use of watermarks embedded on the product package insert or the label materials. Lastly, embossed or raised printing is still being employed.

Covert markers

Covert markers are package markers which cannot be seen by the naked eye. These include invisible inks, embedded micro-wires or magnetic threads and hidden computer chips. The most common types of covert markers are invisible inks. Invisible inks respond to different light frequencies and can only be read using the correct light source. The major advantage of invisible inks is that they can be printed on top of visible ink printing so that package designers do not need additional "real estate" to use them. However, many companies employ invisible inks on the inside of the package and on closure flaps and covers. To keep counterfeiters at bay, some companies periodically change the invisible ink colour and change where invisible ink appears on product packaging. Other techniques such as magnetic threads and micro-wires hidden in the packaging and labels can be read using a scanning device. Hidden computer chips placed behind the product label or within package material are becoming more common. These chips, which are commonly referred to as RFID (radio frequency identifier) chips, produce or reflect a radio signal which transmits a product's authentication identification number to a nearby receiver.

Forensic markers

Pharmaceutical companies are using two methods of forensic markers, taggants and nano-encryption. Taggants are very small amounts of a chemical inert substance placed within the drug product. Because they are only known to the company manufacturing a product, they act as a unique identifier and simplify analyses which can distinguish authentic products from counterfeit products. The FDA has a long list of approved substances that can be used as product taggants.

Another form of forensic marker, nano-encryption, is a layered approach primarily used on the outside of unfilled capsules. The outer layer of a nano-encrypted marker is overt and can be read with a microscope, while the inner layer is covert and requires a special reader which contains specific information about the product and company.

Fighting counterfeit medicines

Significant efforts have been seen during 2013 and 2014 in the fight against counterfeit medicines. Counterfeiting and diversion cases may be rising, but international authorities are improving detection and prosecution of prescription drug counterfeiters and are working diligently to close illegal pharmaceutical manufacturing facilities and illegal online drug sellers. Countries across the world are strengthening regulation and criminal codes around counterfeiting, and private companies are implementing innovative packaging and tracking methods that resist forgery. Fake medicines remain a threat to public health, but with international cooperation everyone involved in manufacturing, distributing and dispensing prescription medications can help deter these crimes.

About the Partnership for Safe Medicines

The Partnership for Safe Medicines (PSM) is a coalition of over 70 organisations that represents patient



advocates, healthcare professionals and every part of the supply chain from manufacturing to distribution to retail. PSM is committed to keeping patients safe from counterfeits and unsafe medicines by maintaining the integrity of the drug supply chain around the world. Keep up with the PSM through our webpage, www.safemedicines.org, or via twitter at @SafeMedicines.

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GREEN ANALYTICAL CHEMISTRY IN THE PHARMACEUTICAL INDUSTRY

by Sergio Armenta and Miguel de la Guardia*

The importance of greening the analytical methods employed in the pharmaceutical industries is highlighted by suggesting the use of several strategies based on: i) direct analysis of samples without any previous treatment, ii) miniaturisation, and iii) automation of procedures. Additional advantages of those methodologies includes the reduction of the environmental impact and operator risks on using the analytical procedures, always taking into consideration that the main objective of analytical chemistry is to solve the problems, but with the lowest possible environmental side effects.

Miguel de la Guardia is full Professor of Analytical Chemistry at Valencia University, Spain. He has published more than 500 research papers and supervised 35 PhD thesis. He has published and edited several books in the fields of green analytical chemistry and food analysis.

Sergio Armenta is a Professor in the Analytical Chemistry Department, University of Valencia. He has authored over 100 peer-reviewed publications. His main research is focused on green analytical chemistry, and the development of new analytical methods based on vibrational spectroscopy and ion mobility spectrometry combined with multivariate data analysis methods.

Green analytical chemistry

Analytical chemistry concerns the maximisation of information obtained from samples in order to solve problems related to the structure and composition of the matter. So, it can be considered that each analytical method is a system in which the inputs are samples, reagents, previous information, energy and labour consumption and the outputs are the obtained data and answers. However, analytical methods also generate waste and emissions. In short, such methods provide information in order to solve problems, but also extra costs for an organisation and risks for both operators and the environment^{1,2}.

Green analytical chemistry attempts to avoid, or at least reduce, the deleterious side effects of analytical methods by replacing

toxic reagents with innocuous ones; reducing the consumption of solvents, reagents and energy; and avoiding toxic waste generation. Therefore, it provides an ethical agreement with the environment and workers' safety and also offers exciting possibilities for the reduction of analytical costs by decreasing the working scale and carefully controlling consumption^{3,4}.

Analytical chemistry in the pharmaceutical industry

The pharmacopoeias define requirements for the qualitative and quantitative composition of medicines, the tests to be carried out on medicines and substances, and the materials used in their production. The objective of the pharmacopoeias is to provide common standards to control the

quality of medicines and substances used to manufacture them. The production of pharmaceuticals and the strict control required is really exigent for lot-by-lot production; the main reason for the introduction of analytical methods in the quality control of products is the need to achieve the narrow variation of $\pm 10\%$ of the nominal content of active principles in formulations. However, the final product analysis must be just a confirmation of the correct function of the whole process, and to achieve this, the quality control of raw materials and the process itself is mandatory to avoid losses and to guarantee the competitiveness of the enterprise.

Therefore, raw materials and process evaluation, together with the final product must be analysed. The process analytical technology (PAT) initiative was first proposed by the US Food and Drug Administration with the objective of achieving significant health and economic benefits by application of modern process control and tests in pharmaceutical manufacturing⁵. The main goal of PAT is the design, analysis and control of manufacturing through timely measurements of critical quality and performance attributes. It involves raw and in-process materials and processes in order to ensure final product quality. The PAT framework comprises risk management and the use of at/on-line sensors that help in monitoring/controlling/designing of the processes. In this sense, a variety of analytical techniques have been used in the pharmaceutical industry, including Fourier transform infrared (FTIR) spectroscopy⁶, UV spectroscopy⁷, near infrared (NIR) spectroscopy⁸, gas chromatography⁹ and high performance liquid chromatography¹⁰.

Moreover, the accomplishment of the legal frame regarding both working conditions and environmental safety forces the assessment of the quality of indoor and outdoor air and the generation of liquid and solid wastes. An additional goal of the analytical control of wastes can be found in their valorisation.

As can be seen in **Figure 1**, it is



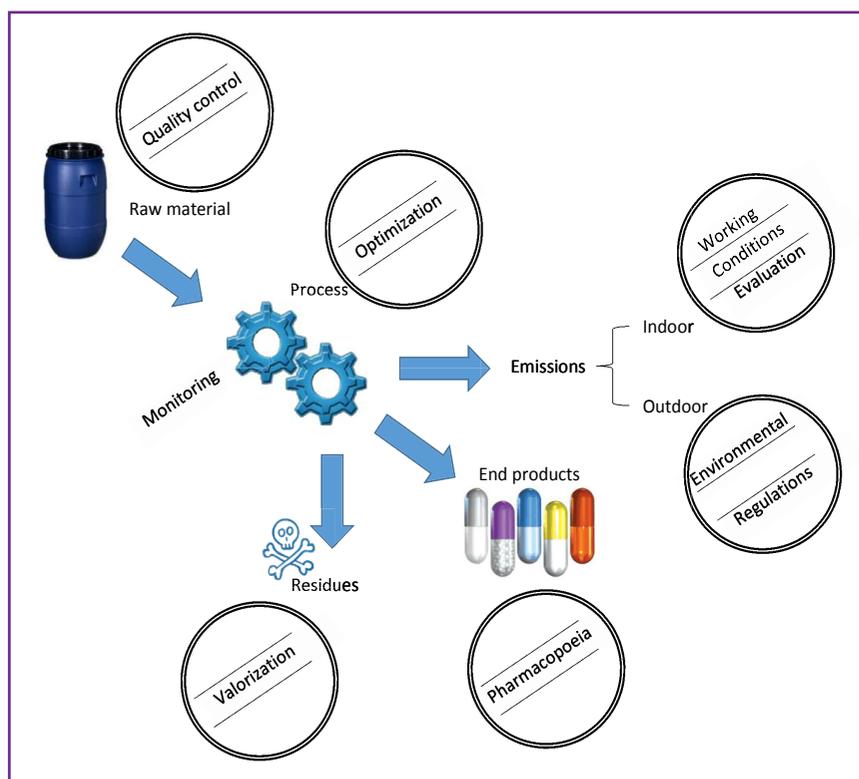


Figure 1: Analytical needs in the pharmaceutical industry.

clear that pharmaceutical industries use several analytical procedures and it invests in labour, reagents, instrumentation and energy consumption. Therefore, analytical activities in the pharmaceutical industry need to be greener in order to extend their use and to reduce extra costs.

Greening pharmaceutical analysis

Sustainability^{11–13} is the main term employed in the literature to avoid the deleterious side effects of pharmaceuticals and industrial activities in this field. It is great that the synthesis and development of new active principles have had a tremendous effect on our life expectations and its quality. However, the input of chemicals into the environment due to the pharmaceutical industries must be reduced. To do this, advances in the greening of technical approaches, together with efforts in education and training, are required in the short term, keeping in mind the development of benign compounds with an easy and fast degradability

after use.

The improvement of pharmaceutical synthesis, together with the use of renewable feedstock, are probably the main strategies for the benign-by-design sustainable pharmaceutical development. However, we cannot forget the importance of analytical tasks in the monitoring and control of all steps, and the efforts on greening pharmaceutical analysis can reduce the environmental impact of chemicals and contribute to the education of people involved in pharmaceutical activities. For instance, innovations in process analytical chemistry and the ability to obtain and analyse large amounts of data have served as the key drivers for greening analytical determinations in the pharmaceutical industry⁵.

Sample treatment is one of the most energy consuming and contaminating analytical steps. It is clear that one of the best ways for greening analytical methods would be to avoid the sampling and sample treatment steps, thus reducing, at the same time, the use

of large amounts of organic solvents, waste generation and energy consumption. In this sense, spectroscopy provides a useful example of a green analytical technique for raw material analysis, process control (temperature in the extrusion step, particle size distribution in the milling process, coating thickness, etc.) and end product quality.

The miniaturisation of methods related to raw materials, process and end product control offers a simple way to minimise reagents, energy and labour and may only affect the representation of obtained data. A clear example of miniaturisation in the pharmaceutical industry is the introduction of ultra high performance liquid chromatography. The reduction of particle size and column dimensions allow the implementation of high throughput applications where the drastic reduction of the run time with an acceptable resolution of critical pairs is the main goal to be achieved¹⁴.

The automation of analytical methods and the use of easy portable instrumentation can also improve the analytical information by reducing the energy and reagents consumed. So, in spite of the absence of suitable direct methods that can be employed without any sample treatment or by using totally innocuous reagents, the aforementioned strategy could be employed as a preliminary approach for greening the main analytical tasks (see **Figure 2** for some of the effects of greening analytical methods in the pharmaceutical industry).

On the other hand, it must be taken into consideration that the development of cheap, fast and green methods related to active principles will improve their use in aspects regarding the quality of the working environment and control of emissions and wastes and it will, surely, open new possibilities for the valorisation of residues.

Additionally, incorporation into the methods of on-line waste treatments will also contribute to

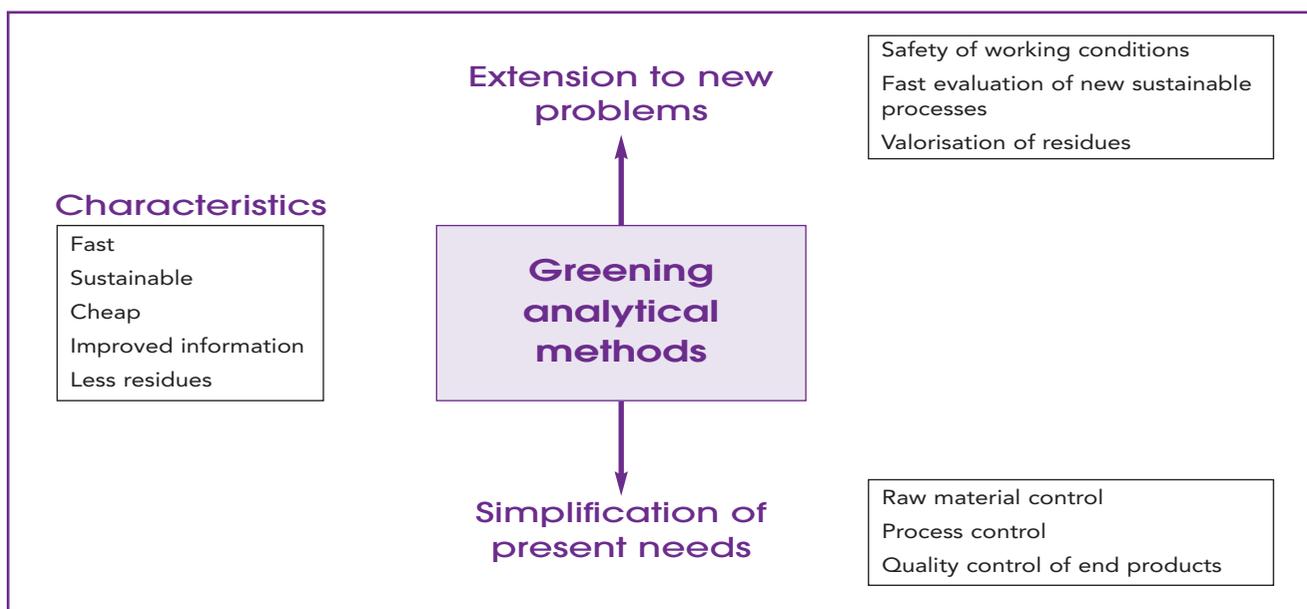


Figure 2: Effects of greening the analytical methods in the pharmaceutical sector.

reduced costs for their external treatment, which offers new opportunities for both education of workers and reuse of employed chemicals.

Perspectives and future trends

Advances in green pharmaceutical analysis will be based on the fact that green methods can be cheaper, safer and more sustainable than traditional ones. Thus, a renovation of quality control strategies in the pharmaceutical industry can be expected based on:

- i) the extensive use of portable instrumentation,
- ii) direct methods of analysis without requiring sample treatment,
- iii) miniaturisation,
- iv) automation of the used methods, and
- v) the incorporation of on-line decontamination processes for the *in situ* treatment of wastes after the measurements.

However, the most exciting future trends in this field will be the extension of the analytical possibilities due to the safety and environmental nature of the methods and thus the possibility to extend the analytical measurements

employed nowadays to other aspects, such as those concerning the quality control of working air, the evaluation of reactor cleaning between batches and the valorisation of residues. This will offer new opportunities of business to the enterprises. Additionally, the tremendous advances in computation and chemometrics will offer new possibilities for the improvement of the information to be obtained from spectroscopy measurements in order to save time, reagents and costs in multianalyte determinations.

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PLANNING YOUR FIRST YEAR OF SELLING IN THE US LIFE SCIENCES MARKET

by Jim Worrell

Jurgen Wettler, CEO of a German manufacturer of pharmaceutical grinding equipment, sat in his office pouring over the recent sales figures from his US subsidiary. They were not encouraging. First year sales were expected to be approximately \$2.3 million. Mr. Wettler was looking at sales of just under \$900,000. What went wrong?

Jim Worrell (jworrell@ameristart.com) is CEO of AmeriStart, a sales and marketing company specialising in the life science industry. He has a degree in International Marketing from Miami University and has held management and marketing positions in Ghana, the Caribbean, The Netherlands and the US. Jim's specialty is sales, marketing and distribution strategies in the US and international markets. He founded AmeriStart in 2003, which has clients in more than 20 countries.

Such is the experience of many life science companies who seek to "strike it rich" in the lucrative US market. It does not have to be that way. With some advance planning, the right expectations, and adaption to the local market, the US market can be a significant part of European companies' sales and profits.

This article will assume you are starting from scratch in month 1. The more you can get done before you open your office (or hire a business development firm), the faster you will realise sales revenue.

First quarter, months 1-3

Smart companies will begin with a well-developed strategy and a good understanding of the market. The objective in the first year is to establish a base, not necessarily to make a profit. In fact, most companies would be pleased if they broke even or even lost a little money as long as they were positioning themselves for the long term.

During these first months, you must answer the following questions and develop the necessary tools that your marketing and sales representatives need to succeed.

1. What products or services are you going to sell to the Americans, and do you know they will buy them?

This seems pretty evident, but a closer look at both the market and your competition may tell you a different story. Products or services that are selling well in Europe may not be received the same way in the US. In our example above, Mr. Wettler found that he could not sell his high-end machines in the US because the American's have a 3-year obsolescence cycle, actually selling older machines and replacing it with newer technology. So selling a product "that lasts 20 years" was not well received by the Americans.

2. How are you different from the competition?

Remember you are competing with companies from all over the world, many with more resources than you. You must have a "USP" or Unique Selling Proposition. Often, this is not easy to identify. You need to dig deep and get creative. Once you have this USP developed, it must be put on all your sales and marketing

materials. And to reference the example above. Mr. Wettler thought his USP was German engineering and quality "to last 20 years", not recognising that this is not what the American customers want to buy.

One way to be different is to solve a unique business problem that your competition has not yet identified or addressed. If you are selling machinery, this unidentified problem might be helping your client recycle his old machinery. It might be working for him to keep stock of spare parts on his premises. If you are selling drugs, it might be a unique packaging that speeds fulfillment, or an easy way to order your products. *Look for business problems, then solve them.*

3. What is your marketing plan and how much will it cost?

The US is larger than all of Europe and travel is expensive. Trade shows are the best way to meet new customers, and Americans are more receptive to working with new suppliers, so you need to be visible at these shows. Shipping trade show materials and staff from New York to California to Houston to Miami can be expensive.

You might also base your marketing and sales program around geography. Keep in mind that it takes one full day of travel to fly from the West coast to the East coast because it is a 5-hour flight and you lose 3 hours in time zones. You may be able to meet your sales forecast based only on companies in New York, New Jersey, Pennsylvania and Connecticut. All of these states are in a relatively small area and can be reached by automobile. One Scottish customer we worked with identified enough biotech and pharma companies in these four states that he saved thousands of dollars and months of travel time by concentrating on prospects only in this area.

4. Who are your target accounts?

You should have a list of 100 prospects identified IN



ADVANCE. This includes the name of the company and the name of the individuals you want to call on. Don't show up and tell the business development representatives to "go find customers". Building a target database takes time and effort, but it can be done. With a "hit list" in hand, your business development representatives will be much more productive.

5. Americanise your marketing materials

Imagine a US company selling in your native country using brochures with incorrect German, Italian or French. The native customers would not take them seriously. Hire a good agency and make sure you have proper American English. This goes for your user manuals and technical manuals as well.

6. Think like an American (or hire good American staff)

I recently had the CEO of an Indian company tell me "Our executive team is not using LinkedIn, because this is not in our culture". He was overlooking the fact that LinkedIn is the most powerful business tool in America, and *not* to be there puts his company at a clear disadvantage.

Quarter 2, months 4-6: be active, visible and build relationships

The key to success in the US market (and any global market for that matter) is to be active and visible. Do not let your sales representatives hang around the office and just make phone calls. Get out in the market and build relationships. Your business development staff should understand the problems US companies face and develop solutions to solve these problems.

The problems and solutions may be different than those of European customers, but you will never know until you get out and talk to people.

Go to trade shows, seminars and other industry events. Hire a good public relations firm to get your name in multiple magazines and websites. Write articles, blogs and be active in social media. Send out mailers and write white papers about industry issues. Become a thought-leader to the 100 companies on your target list.

By month 4, 5 or 6, you should begin to see the results of your efforts and requests for proposals should start coming in. Recognise that while American companies are quick to try new resources, they may start with small orders to "test the waters" of a new supplier. Your job is to ensure that this first order exceeds their expectations. Do whatever it takes to make your customer say, "WOW, these guys are good!"

Americans are service-oriented and no matter what industry you are in or what products you sell, you are in the service business. Always keep in mind that, while it's great to get the first order, it's the *second* order that is the most important.

Months 6-12

If you have done your job correctly in the first 6 months, these next 6 months are focused on delivering your first sales and continued emphasis on building the business. Follow the steps below.

1. Continue to identify new prospects. Always keep the top of the sales funnel full.
2. Refine your marketing position and message. Based on what you are learning from your first sales calls and first orders, don't be afraid to "pivot" or change the message on your website and

marketing materials. You may discover a niche that others have overlooked.

3. Take care of your first customers. This cannot be overstated. Customers come first!
4. Once you have a customer and have delivered your first orders, begin to go deeper into these accounts. Look for more ways to add value to these first customers. Look for initiatives in their companies where your product or service fills a need. Look for additional business problems they have based on your growing relationships with the clients.
5. Get your senior management involved in these accounts. Once your business development representatives have opened the door and even delivered the first order, make it a point to have your directors visit these clients. Americans like to know that their business is important enough to warrant a visit from your Managing Directors. And often, the Managing Directors will be able to spot opportunities that the business development representative may not have seen. Once they spot these opportunities, he or she has the authority to take action back in Europe to ensure the company delivers on these opportunities to maximise sales to the US customer.

As a final thought: be patient. Be willing to invest for the long term. Take the time to learn the market, adapt your products and your marketing message, build relationships and solve business problems by delivering value. Rome was not built in a day. Neither is the American market.



THE POWER OF DRUG COLOUR

by Tessa Fiorini Cohen

A pill's hue can affect how it's judged by patients, how it's marketed, and even how well it works.

Tessa Fiorini Cohen is a pharmaceuticals professional with over 5 years' experience in industrial research and development. She currently works in quality assurance, with a focus on process validation and minimisation of product cross-contamination risk. She also works as a freelance science writer.

The first time drug kingpin, Tuco Salamanca, tries Walter White's characteristically blue meth on the AMC drama *Breaking Bad*, his priorities are straightforward: he doesn't care about colour, he just wants to get high. "Blue, yellow, pink, whatever man," he says. "Just keep bringing me that!"

But as fans of the show already know, White's business soon becomes all about the blue—from drug addicts to rival producers, everyone wants White's signature tint.

The fictional meth manufacturer isn't the only one who understands the importance of drug colour—on both sides of the law, it's a key part of branding. Viagra is famously known as "the little blue pill", Nexium is marketed as "the purple pill", and street names for illicit drugs run through the whole rainbow. But there are also subtler and arguably more important roles for drug colourants. They're not there just to make a drug look pretty.

Tuco may have been surprised to learn, for example, that meth of a different colour may have improved his high. Studies have shown that we associate drug colours with specific effects that stretch far beyond brand recognition. Once we've tricked our brains into making the association, it actually becomes real. The placebo effect comes into play and the drug is more effective.

Imagine burning your skin and treating the pain with a cream. Is your imaginary cream white? Now picture it red. Would you trust the

cream to work as well? If you had a moment of pause there, you're not alone. Multiple trials—some with placebos, others with active drugs—have shown that patients' colour-effect associations can impact a drug's efficacy by measuring physical signs like heart rate and blood pressure.

Pharmaceutical companies are well aware of these associations and carry out extensive related research

when developing new products or rebranding old ones.

Food colour trumps flavour

Blue pills, contrary to what *Breaking Bad* may have you believe, act best as sedatives. Red and orange are stimulants. Cheery yellows make the most effective antidepressants, while green reduces anxiety and white soothes pain. Brighter colours and embossed brand names further strengthen these effects—a bright yellow pill with the name on its surface, for example, may have a stronger effect than a dull yellow pill without it.

When researchers take culture into account, things get a bit more complicated. For instance, the sedative power of blue doesn't work on Italian men. The scientists who discovered this anomaly think it's due to 'gli Azzurri' (the Blues), Italy's national soccer team—because they associate the colour blue with the drama of a match, it actually gets their adrenaline pumping. And yellow's connotations change in Africa, where it is associated with



better antimalarial drugs, as eye whites can turn yellowish when a person is suffering from the disease. (Interestingly, this is the opposite of the norm. Just like with the burned-skin example, drugs usually work better when their colour matches the intended outcome, not the symptoms of the condition they're treating.) Such cultural variances are one reason why a drug may appear totally different in separate countries.

Colour also has a more practical role in drug manufacturing. In light-sensitive products, tints can lend opacity, keeping active ingredients stable. Colour, together with shape, also aids drug recognition. This ensures that drugs aren't mixed up during production or packaging—a

scenario that would have terrible repercussions for patient safety as well as brand reputation. And colour's role in drug recognition is equally important at the patient level, preventing accidental overdose by helping patients on multiple drugs to recognise each one. This is most relevant to the elderly, who are often on multiple drugs and may be dealing with complications from eyesight degeneration or dementia. It is also a bonus to healthcare workers, who have to give out lots of different drugs in a short space of time. Colour's role here shouldn't be taken lightly; five percent of all United States hospital patients receive incorrect medication.

But colour-effect associations can

also backfire—while a drug's hue acts as a mental imprint, reminding people to take their medications, this also means that patients are also likely to stop their medication regimen if drug colours are changed. This is one of the reasons why drug manufacturers ferociously guard their designs and colours with patents, and generic companies try so hard to resemble them.

So no matter what Tuco Salamanca may say in a moment of meth-induced euphoria, the choice between blue, yellow or pink actually matters quite a bit—and it's anything but random.

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Expert Guidance on Industrial Pharma Microbiology

Edited by Geoff Hanlon and Tim Sandle

Industrial Pharmaceutical Microbiology: Standards and Controls

provides clear, practical and up-to-date guidance for handling virtually every compliance and operational challenge associated with pharmaceutical microbiology.

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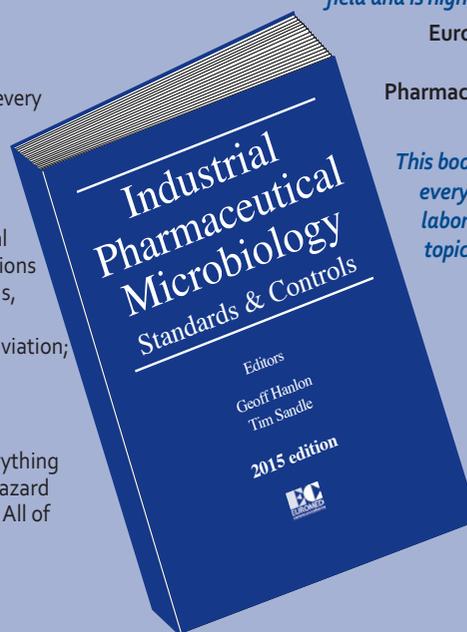
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IRELAND LAUNCHES AN INTEGRATED 5-YEAR PHARMACY EDUCATION AND TRAINING PROGRAMME

by Maura Kinahan

In recent years, the Pharmaceutical Society of Ireland (PSI) has prioritised pharmacy education reform and commissioned a root-and-branch review of the 5-year MPharm programme – the PEARs (Pharmacy Education and Accreditation Reviews) project (published in 2010). A key recommendation of the PEARs project was the introduction of a 5-year fully integrated Master's level of education and training for those seeking to become pharmacists, replacing the current 4+1 model. This restructuring of the pharmacist qualification will commence with effect for programme entry in September 2015.

Maura Kinahan is an industry-based pharmacist who has been involved in National Forum for Pharmacy Education and Accreditation, which advised the PSI on the rollout of the integrated MPharm programme, and is still involved in the National Steering Committee to support the Schools of Pharmacy in the rollout of the programme from September 2015. She is also a PIER committee member leading on education and membership.

This new programme will involve the integration of the curriculum to support the dispersal of practice placements throughout the 5 years (rather than concentrated in the final year). The three Schools of Pharmacy in the Republic of Ireland (Royal College of Surgeons of Ireland (RCSI), Trinity College Dublin (TCD) and University College Cork (UCC)) have developed new curricula to facilitate experiential learning throughout the 5 years of the qualification. These changes will enable placement experience of varying duration in the three main practice settings of community, hospital and industry (shadow placements in the second year, a 4–6-month placement in the fourth year (industry placement can only take place here), and an 8-month patient facing placement in the fifth

year). A joint shared services office hosted in one of the schools will be set up to support the placement aspect of the programme.

Considering the extensive pharmaceutical, biopharmaceutical and medical devices industries in Ireland (circa 50K employed directly), the number of industry-based pharmacists is low (circa 300). One of the main reasons for such low representation was the fact that there was only one School of Pharmacy (TCD) graduating a small number of pharmacists for many years who were actively recruited into community pharmacy by high entry level salaries. This has changed in recent years with RCSI and UCC now providing pharmacy education (170–180 pharmacists qualify each year). Also, many pharmacists who qualified overseas

now practice in Ireland.

The number of current industry intern placements is small (approximately 20 industry training sites approved by PSI). One of the main barriers to increasing the number of intern placements has been the legislative requirement (Pharmacy Act 2007) to have an on-site pharmacist tutor supervising the pharmacy intern day-to-day. Many of the Irish manufacturing sites do not employ pharmacists on-site because the qualified person does not need to be a pharmacist, as is usual in most European countries. The Pharmacy Act 2014 allows much more flexibility in terms of day-to-day supervision for non-patient facing placements, and allows for overseas placements, which will open up many more intern opportunities.

PIER (Pharmacists in Industry Education and Regulatory) was set up in 2012 to represent the interest of all Irish pharmacists employed outside of the traditional patient-facing roles. Since TIP/TIPPSA (previous interest group for Irish industry pharmacists and pharmaceutical scientists) disbanded, there had been a void in terms of a recognisable industry pharmacist group in Ireland for students and young pharmacists to engage with. PIER has organised a number of industry careers events over the past couple of years to raise awareness of the many industry roles that a pharmacist can hold. It has been encouraging to see the level of interest at these events. The committee is also actively working to increase the number of summer and intern placements in the short to medium term. PIER has committed to working with the three schools to help them deliver industry aspects of the integrated MPharm programme through facilitated workshops, shadow placements, site visits and an increased number of intern placements.

For further information on the fully integrated MPharm programme, please see <http://www.thepsi.ie/gns/education/fiveyearintegratedpharmacydegreeprogramme.aspx>



EPSA INDIVIDUAL MOBILITY PROJECT - A STEP INTO A PROFESSIONAL CAREER

by Svetlana Kolundžić

The European Pharmaceutical Students' Association (EPSA) Individual Mobility Project (IMP) is a long-term internship project that gives the opportunity to students and recent graduates from all EPSA member associations to gain an additional real-time work and research experience in any field of pharmaceuticals. It is a unique network developed to offer international professional experience for students who have strong professional and personal ambitions as well as to those who are undecided or confused about their professional future path and wish to explore the opportunities in any kind of pharmacy-related professions.

The EPSA represents more than 160,000 students and recent graduates from 36 European countries. The Association has a permanent office in Brussels, Belgium and conducts its activities through regular congresses, advocacy activities, training events, publications, exchange programmes and virtual presence. The main aim of EPSA is to develop the interests and opinions of European pharmacy students and to encourage contact and cooperation between them. EPSA is actively engaging at student and professional level, bringing pharmacy, knowledge and students together and encouraging personal development.

The IMP is performed in collaboration with IMP partners who offer the placement. An IMP partner can be any company or institution supporting the EPSA IMP and European pharmacy students by providing them with vacant place(s) in work or research connected to any field of pharmacy and pharmaceutical sciences. Throughout the years, we have managed to collaborate with many different pharmaceutical companies, universities and agencies active in healthcare policies.

Placements are arranged for a period of 3 to 12 months with an appropriate salary to cover basic living costs in the country where the internship is performed. Promotion of the placement is advertised over EPSA's internal communication network as well as on the EPSA website and social media. This ensures that not only a high number

of students and recent graduates are reached, but also promotes the work, the working environment, the image and the values of the IMP partner among European pharmacy students. Based on mandatory and preferable qualifications for the trainee set by the IMP partner, EPSA pre-selects applicants thus providing to the IMP partner the best candidates for the position. The IMP partner makes the final decision in the selection process.

One of the EPSA members, Helena Vankatova from the Czech Republic, shares her experiences from an IMP placement in the EMEA (Europe, Middle East, and Africa) Consumer Healthcare Sales team in the GlaxoSmithKline (GSK) office in London, UK. She started her 12-month internship in February 2014.

"The offered position was within the EMEA sales team especially



focusing on expert marketing. The main reason I applied for the role was my passion for pharmacy and lack of expertise in this particular field. The role description seemed to be a perfect fit to my desire to develop into a versatile pharmacist who can contribute to the well-being of patients.

After graduation, I started working as a pharmacist at the community pharmacy. Gaining almost 2 years of experience in direct contact with patients helped me strengthen the knowledge learned at university and develop into a confident expert. Using this insight significantly sped up the transposition to the pharmaceutical company environment, since many things started clicking together and my expert opinion has been valued at all times.

The main responsibilities of the project involved coordination between individual and team work projects, maintenance of the partnership between EPSA and GSK, collaboration with UK pharmacy students, coordination of various market requests for localising Expert Marketing eDetailing Sales content, and overseeing mandatory actions required for the European Federation of Pharmaceutical Industries and Associations (EFPIA) Code reporting."

Additionally, the IMP represents a unique opportunity for students and recent graduates to gain valuable experience about foreign European countries, their customs and cultures, as well as to learn and get to know European diversity, which are the attributes often encouraged



by the European Commission. Helena explains what she gained out of IMP.

"During the year, I have been exposed to challenging situations which have had a positive impact on personal development and experience gaining. I have evolved effective ways of thinking and fast reaction to tasks, efficiency, built strong self confidence especially at training delivery, knowledge transfer, and international meeting speaking. The opportunity to meet colleagues from various markets helped to create stronger and trusted business relationships.

I would encourage every student

and recent graduate to use the opportunities the IMP are offering. Starting with the application process, interviews and fulfillment of the requirements, this programme takes individuals out of their comfort zone. Once you are selected, you are going to learn many new things in the role, and also get to know yourself better while being challenged by situations you have never experienced before. From a professional point of view, the IMP offers a unique way to start a career you desire."

IMP partners consider the EPSA IMP as a great source of young, motivated and talented trainees and

are very satisfied with the level of communication, updates and notifications received from EPSA while arranging the training placement. Trainees tend to be able to work independently, with excellent English communication skills, a high level of aptitude in the working environment, and show professionalism and knowledge. Because of that, many of our partners choose to continue with the IMP and deepen collaboration with EPSA.

For more information about EPSA and the IMP, visit the EPSA website (www.epsa-online.org) or contact the Vice President of Mobility, Domen Kutoša (vp.mobility@epsa-online.org).

PharmacoVigilance Review

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Editor – Rob Begnett

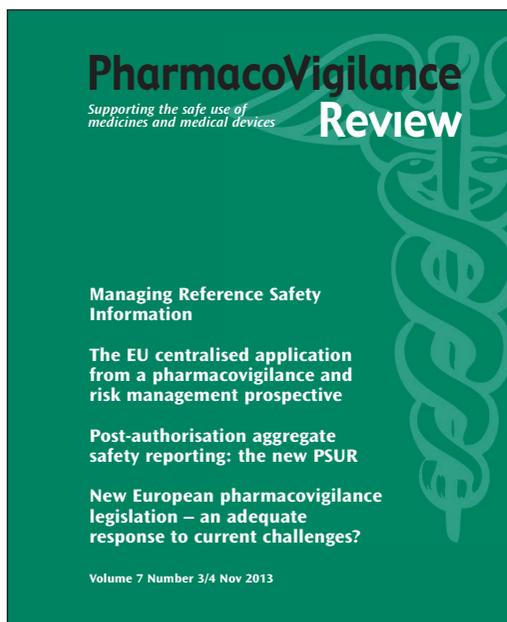
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regulatory review

The current review period has seen a number of changes in the regulation of medicines and regulatory guidance in the EU, International markets and the USA

USA

Launch of Office of Pharmaceutical Quality (OPQ)

This new Center for Drug Evaluation and Research office creates a drug quality program as robust as the programs the agency already has in place for drug safety and efficacy. The OPQ will streamline the Food and Drug Administration (FDA) processes that monitor drug quality throughout the product lifecycle.

SUPAC: Manufacturing Equipment Addendum

This combines and supersedes certain scale-up and post-approval changes (SUPAC) guidances. It removes the lists of manufacturing equipment that were in affected guidances and clarifies the types of processes being referenced.

Product Tracing Requirements Compliance Policy – Guidance for Industry

The FDA recognises that some manufacturers, wholesale distributors and repackagers may need additional time to work with trading partners to ensure that all required information is provided. To minimise supply disruptions of prescription drugs, the FDA does not intend to take action against trading partners in such cases prior to 1 May 2015.

FDA letter stating that bioequivalence study protocols contain safety protections comparable to the applicable risk evaluation and mitigation strategy (REMS) for the reference listed drug (RLD)

This draft guidance describes how a prospective abbreviated new drug application (ANDA) applicant may request a letter stating that the FDA

has determined:

(1) the applicant's bioequivalence study protocol contains safety protections comparable to those in the REMS with elements to assure safe use applicable to the RLD, and

(2) that the FDA will not consider it a violation of the REMS for the RLD sponsor to provide a sufficient quantity of the RLD to the generic firm or its agent to allow the testing necessary to support its ANDA.

Conclusions of the FDA-EMA (European Medicines Agency) parallel assessment of quality-by-design elements of marketing applications

The US FDA and the EMA are publishing a series of joint question-and-answer documents that outline the conclusions of this first parallel assessment.

“Accidental” administration of trial materials to patients

The FDA has become aware that some training intravenous products have been distributed to healthcare facilities and subsequently administered to patients. There have been reports of associated serious adverse events.

(Readers should note that it is important to ensure via the quality system that products which were never intended for human use, e.g. demonstration/training kits, placebo from process/machine trials cannot enter the legitimate supply chain in such a way that they can be administered to patients. MH)

Europe

Guideline on Setting Health-Based Exposure Limits for Use in Risk Identification in the Manufacture of Different Medicinal Products in Shared Facilities

This final version comes into effect on 1 June 2015 and links in to the new versions of Chapters 3 and 5 of the EU GMP (good manufacturing practice). The approach is to review and evaluate pharmacological and toxicological data of individual

active substances to enable determination of threshold levels as referred to in the GMP guideline. These levels can be used as a risk identification tool and also to justify carry over limits used in cleaning validation.

Guideline on Similar Biological Medicinal Products

This final guideline, effective on 30 April 2015, describes and addresses the application of the biosimilar approach, the choice of reference product and the principles for establishing biosimilarity.

Delegated Regulation (EU) No. 1252/2014 GMP for Active Substances for Medicinal Products for Human Use

This document provides the necessary legal framework of GMP principles for active pharmaceutical ingredients (Part II of the EU GMP Guide delivers further detail of these principles). The regulation, valid since May 2014, only came into force on 15 December 2014 and is directly applicable in each EU member state without a transitional period.

Adaptive pathways: a future approach to bring new medicines to patients?

The concept of adaptive pathways foresees an early approval of a medicine for a restricted patient population based on small initial clinical studies. The first approval is followed by progressive adaptations of the marketing authorisation to expand access to the medicine to broader patient populations based on data gathered from its use and additional studies.

Mitigating risks due to the use of antibiotics in animals

The EMA has published recommendations to limit the development of antimicrobial resistance linked to the use of antibiotics in animals. It focuses in particular on promoting the responsible use in veterinary medicine of antibiotics that are critically important in human



medicine, e.g. fluoroquinolones and third and fourth generation cephalosporins.

PharmEuropa proposed texts – tablets

This proposed text requires that tablets with break-marks must be functional and their efficacy assessed in respect of uniformity of mass of the subdivided parts.

Medicine and Healthcare products Regulatory Agency (MHRA)

GMP Data Integrity Definitions and Guidance for Industry

This document provides MHRA guidance on GMP data integrity expectations. It complements existing EU GMP, and should be read in conjunction with national medicines legislation and EU GMP.

MHRA helps pharmaceutical companies develop European (UK) innovative technology sites

MHRA advised both ESAI and Astra Zeneca on the regulatory requirements needed for the innovative concepts and design

philosophies. One of the processes involved includes multiple aseptic stages.

(Companies so often design first and then grumble when the regulator finds fault with design – this approach is much more sensible – MH)

Medicines distribution in the maritime sector

From 1 December 2014, any company continuing to wholesale such medicines without a WDA(H) will be liable to enforcement action.

International

Australia & New Zealand Cessation of efforts to establish a joint therapeutic products regulator (Australia New Zealand Therapeutic Products Agency)

This decision was taken at Government level following a comprehensive review of progress and assessment of the costs and benefits to each country.

Pharmaceutical Inspection Cooperation Scheme (PIC/S) Establishment of PIC/S

Inspectors Academy (PIA)/dedicated facilities seminar outcomes

PIC/S is to establish the PIA. This initiative to set up a web-based educational centre aims at harmonising and standardising GMP training at an international level through an accredited qualification system.

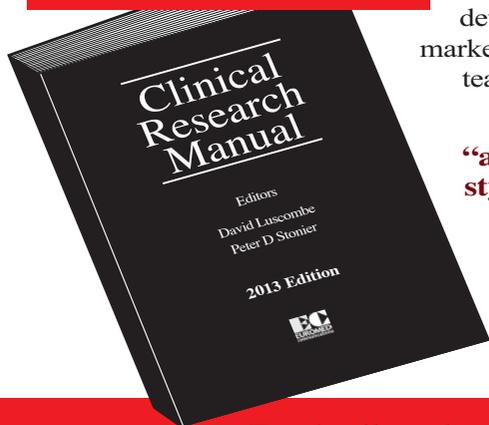
PIC/S also agreed to establish a PIC/S Expert Circle on Dedicated Facilities, which will draft an Aide Memoire on the inspection of dedicated facilities, and provide training to inspectors on this difficult issue. As much as 60% of all inspectors have not received any training in this critical field: as a result, the Expert Circle will work on creating such a training programme for inspectors.

For further information on these and other topics we suggest you refer to the websites of relevant regulatory bodies and to current and past editions of "GMP Review News" published by Euromed Communications. To subscribe to this monthly news service contact info@euromedcommunication.com

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bottled brown

Broken

"Something about the supply chain is broken," said the community pharmacist. "I spend half my time sourcing things."

"Pharmacists phone me about three times a day saying that something is out of stock," said the medical general practitioner. "Ordinary things such as generic benzoyl peroxide. I'm having to substitute *Edipuo* or *Duac*. It's a false economy."

Something is amiss with medicine supply in the UK.

The easiest culprit to identify is the government. Governments should be more aware of the impact upon patients. My hunch is that the health professionals attempt to protect patients from knowing about problems. But patients realise that the NHS is struggling financially when crucial scan results, anxiously awaited, are posted second class.

Fortunately, there seem to be fewer problems with the more expensive medicines for serious disease.

"I would be very upset if I could not get my aromatase inhibitor," said one patient.

The European Medicines Agency keeps a list of shortages. Currently, it includes midazolam, imiglucerase, cidofovir, etanercept and macasermin; all affect comparatively few patients.

Governments can lawfully act to reduce the effect of patents if they adversely affect their citizens' lives. Specific governments may compulsorily license medicines.

Indonesia did that for certain anti-HIV medicines; owner companies may receive very low royalties (e.g. 0.5%).

Maybe the British government is paying industry too little under the price regulation scheme. Less income means less money for research into new medicines. Famously, getting a new entity to market is expensive and may take 15 years. Lack of reward may even pose an existential threat to pharmaceutical companies. If the pistons of commerce falter, companies may cease to trade. Then, medicine supply ceases and jobs vanish.

Strategies

To avoid that, industry uses various strategies. They may reformulate; that "evergreens" medicines to extend patent life. Post-launch, product prices may be "modulated". Companies may give away products for a time, or heavily discount to certain markets. Their populace may be unable to afford once the subsidy ceases. These tactics may keep parallel imports at bay. But if the lower price makes the original product financially more attractive than the parallel import, more branded original may be required than can quickly be provided.

World-wide, there may be only one source of an active pharmaceutical ingredient (API); if that dries up, immense problems follow. Manufacturers must then use an API from a new source. However, progress through current good

manufacturing practice and regulatory hoops may be lengthy.

The US company *Gilead Sciences* in 2014 agreed to voluntarily license certain anti-hepatitis C anti-virals to seven India-based manufacturers who would supply to many developing countries, receiving 7% royalties. The alternative may be receiving nothing as those countries could not afford non-subsidised prices. Indeed, a third of the world cannot afford to access essential medicines. I feel guilty about the unfairness of the international distribution of wealth.

I sense you throwing up your hands at such complexity and saying, "Not my problem." But it does tar the whole industry. Let us examine the nature of humankind to see why this is occurring.

Delving deeper

The founding father sociologist Max Weber remains widely respected. He said that there were only four reasons for human behaviour. They are: selfishness or instrumentality, selflessness or altruism (morality fits here), tradition: the great flywheel of society, and affectivity: you so behave because you just like it (e.g. sugaring your coffee because you have a sweet tooth). I have never found a behaviour that they did not cover.

I offer no answer. I expect that your industrial "backyard" is in order. But maybe supply difficulties do merit reflection, including by your movers and shakers.

Malcolm E Brown



news from the EIPG

PHAR-IN

Following completion of the survey on competencies in biotechnology, some in-depth, semi-structured interviews with managers working in the biotechnology industry are being conducted. Simultaneously, the action plans for undergraduate and a postgraduate series of short courses in biotechnology are being developed.

Healthcare workforce

Thomas Lion (VAPI/UPIP, Belgium) will represent EIPG at the forthcoming European Pharmacy Students Association (EPSA) reception, which is supported by Members of European Parliament from Ireland and Romania and to be held in the International Auditorium in Brussels.

EPSA/EIPG seminars

The EPSA and EIPG have recently organised two webinars, internationally accessible as workshops. The following is a report from Adéla Firlová, EPSA Social Services and Public Health Coordinator.

The main topics were the pharmaceutical industry and regulatory affairs with EIPG speakers Dr. Georgina Gál (Hungary) and Prof. Claude Farrugia (Malta). The 164 participants had an amazing

opportunity to learn from these industrial pharmacist professionals and the opportunity was much appreciated. Participants were motivated to join because the topics were of interest to them and students mentioned that they would like to discover job opportunities in the field of industrial pharmacy. Many would like to work in regulatory affairs.

Anni Svala (EIPG Vice-President for Education and Careers) introduced the webinars with a short presentation on EIPG and this was followed by an introduction on EPSA. Prof. Claude Farrugia presented on the "Subject(ion) of Pharma" with the latest trends explained through graphs and charts and followed up by answering a number of questions. Feedback indicated participants felt the talk was clear, detailed and interesting.

Dr. Georgina Gál then presented on a field of pharmacy that is not well known to many students and caused some of them to change their opinion on the possibility of working in Regulatory Affairs. Dr. Gál's presentation brought Regulatory Affairs into the spotlight and participants discovered what it takes to work in this area, how to specialise and how to reach the dream of becoming a Regulatory Affairs Manager. Students had many questions including the possibility of

internships in Regulatory Affairs and what to focus on during pharmacy studies.

Quoting outcomes from students on the webinars:

"The pharmaceutical industry is a victim of the economic crisis, governments want to pay less for their medicines."

"How to follow my dream of becoming part of the regulatory affairs team."

"EIPG is a very interesting association! I am glad there are pharmacists who want to work in and represent pharmacists employed in industry."

"Good to learn what the pharma industry market looks like."

After the webinar, 78% of participants who answered the survey (72 out of 120) stated that they would like to work in Regulatory Affairs, a really motivating number! For future webinars, participants suggested topics such as pharmaceutical marketing, pharmacoeconomics and pharmacovigilance.

We hope that the collaboration with EIPG will continue in the longer term.

Jane Nicholson, Executive Director EIPG, jane@nicholj.plus.com

CALL FOR ARTICLES

Dear Colleague

We hope you enjoy the *European Industrial Pharmacy* and find it both useful and informative.

We are currently seeking new articles for future issues of the journal and would like to invite you to contribute an article or review paper on any aspect of industrial pharmacy to the journal. All issues of *European Industrial Pharmacy* are indexed by both Scopus and Embase and thus are available through the listings for any other industrial pharmacist internationally.

events

MARCH 2015

19 March 2015 – London, UK
Combating Counterfeit Medicines: The Solutions
www.jpag.org

22–25 March 2015 – National Harbor, MD, USA
Pharma Forum 2015
www.cbinet.com

23–24 March 2015 – Amsterdam, The Netherlands
Global Bioequivalence Harmonisation Initiative
www.gbhi.eu

23–25 March 2015 – London, UK
PAT and Quality by Design in Pharma
www.patandqbd.com

24–25 March 2015 – Dusseldorf, Germany
Pharma Congress 2015
www.pharma-kongress.com

25–27 March 2015 – Hamburg, Germany
20th Congress of the EAHP: The Hospital Pharmacist's Agenda – Patient Safety First
www.eahp.eu

APRIL 2015

4–7 April 2015 – Glasgow, Scotland
10th Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology World Meeting
www.worldmeeting.org

13–14 April 2015 – Reims, France
1st European Conference on Pharmaceutics – Drug Delivery
www.apv-mainz.de

14–15 April 2015 – Düsseldorf, Germany
BioProcess International European Summit
www.informa-ls.com

14–15 April 2015 – Berlin, Germany
Aseptic Manufacturing
www.pda.org

16 April 2015 – Sandwich, UK
APS Industrial Insights 2015
www.apsgb.co.uk

16–17 April 2015 – Munich, Germany
Manufacturing of Biologics and Biosimilars
<http://pharma.flemingeurope.com>

22 April 2015 – London, UK
The 14th Joint QP Symposium – QP Responsibilities and the Pharmaceutical Supply Chain
www.rpharms.org

22–23 April 2015 – Chicago, IL, USA
7th Annual World Drug Safety Congress Americas 2015
www.healthnetworkcommunications.com

24–25 April 2015 – London, UK
The Clinical Pharmacy Congress 2015
www.pharmacycongress.co.uk

25–27 April 2015 – Lisbon, Portugal
Conference on the Safety Paradigm for Medicines – Changes and Challenges from Drug Discovery to Usage
www.eufeps.org

MAY 2015

4–7 May 2015 – Frankfurt, Germany
ISPE Europe Annual Conference
www.ispe.org

4–7 May 2015 – Athens, Greece
2nd Annual International Conference on Pharmaceutical Sciences
www.atiner.gr/pharmako.htm

5–7 May 2015 – Berlin, Germany
Global Pharmaceutical Contract Manufacturing Summit
www.gpcmevent.com

5–8 May 2015 – Nice, France
RDD Europe 2015
www.rddonline.com

12–13 May 2015 – Brussels, Belgium
5th Annual Life Science Cold Chain & Temperature Controlled Logistics
<http://pharma.flemingeurope.com>

18–19 May 2015 – London, UK
ADC Summit 2015
www.smi-online.co.uk/pharmaceuticals/uk/conference/adc-summit

18–20 May 2015 – Berlin, Germany
12th Annual Biosimilars Conference
www.informa-ls.com

19–20 May 2015 – Geneva, Switzerland
PIC/S–PDA Workshop
www.pda.org

19–21 May 2015 – Brussels, Belgium
24th Annual EU Pharmaceutical Law Forum
www.informa-ls.com

JUNE 2015

2–3 June 2015 – Amsterdam, The Netherlands
Advanced Therapy Medicinal Products
<https://europe.pda.org>

9–10 June 2015 – Heidelberg, Germany
6th European GMP Conference
www.gmp-conference.org

10–12 June 2015 – Boston, MA, USA
14th Annual World Pharma Congress
www.worldpharmacongress.com

15–17 June 2015 – Geneva, Switzerland
EUFEPS Annual Meeting 2015 – Systems Approaches for Better Medicines and Health
www.eufeps.org

16–17 June 2015 – Switzerland
Pharmaceutical Packaging and Labelling Summit
www.pharmapackaginglabelling.com

23–24 June 2015 – Brussels, Belgium
Quality and Regulation Conference
<https://europe.pda.org>

23–24 June 2015 – Brussels, Belgium
Publication & Clinical Trial Disclosure
www.cbinet.com

25 June 2015 – London, UK
Challenges in Current GMP
www.jpag.org



COMPETENCES FOR INDUSTRIAL PHARMACY PRACTICE IN BIOTECHNOLOGY - THE PHAR-IN PROJECT

by the PHAR-IN Consortium

The PHAR-IN Competences for Industrial Pharmacy Practice in Biotechnology¹ consortium consists of organisations representing industrial employees, viz the European Industrial Pharmacists' Group (EIPG)², the European Federation of Pharmaceutical Industries and Associations (EFPIA)³ and pharmacy academics from the European Association of Faculties of Pharmacy (EAFP)⁴. PHAR-IN is funded by the European Commission via its Education, Audio-visual and Culture Agency; it bears the reference 538252-LLP-1-2013-1-BE-ERASMUS-EKA.

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The aim of the project is threefold:

1. to develop the Delphi methodology for establishing and evaluating a competence framework for biotechnology practice,
2. to propose a framework of competences in biotechnology for future and current industrial employees, and
3. to develop courses necessary for the acquisition of such competences.

A small expert panel consisting of the authors of this paper produced a biotechnology competence framework by:

1. drawing up an initial list of competences, and
2. ranking them in importance using a 3-stage Delphi process.

The framework was next evaluated by a large expert panel of industrial employees and academics drawn

from the EAFP, the EIPG, the EFPIA and the European Federation for Pharmaceutical Sciences (EUFEPS)⁵ with a snowballing effect for recruitment of others. Snowballing led to the participation of pharmacists and others working in areas outside industry and academia.

Results show that the Delphi tool developed can be used to determine a consensus framework of competences with priorities for course development. The competences for biotechnology practice that received the highest scores were those in:

- Category 1 Research and development
- Category 6 "Upstream" and "downstream" processing
- Category 7 Product development and formulation
- Category 8 Aseptic processing
- Category 10 Product stability

- Category 11 Regulation.

Introduction

There is a time gap in knowledge transfer between industry and education. Educational programmes at universities tend to change slowly and, furthermore, are not always in line with practice. This is in contrast to industry. The latter needs to change direction and policy within months in order to remain competitive. This situation requires that the educational system be capable of rapidly offering the right courses to produce the right person with the right competences at the right time. The missing link for such a development is a system whereby universities can obtain rapid feedback from industry on what they should be teaching.

PHAR-IN has developed a Delphi tool for such a feedback process offering a rapid reaction in a quickly evolving field leading to the creation of cutting-edge courses in biotechnology. This paper presents the development of the Delphi tool and the results of the survey on the PHAR-IN framework of competences for practice in the biotechnological industry (see [Questionnaire](#) for the PHAR-IN survey).

Methodology

Delphi technique

Many pharmacy departments continue to use an academic approach to the development of courses that is bereft of sufficient input from stake-holders and end-users, such as industrial employees. If staff are not actively involved in the drug industry, they can become disconnected from recent developments. Even staff that are active in industry may be so specialised as to be unable to grasp all the developments. Several methods have been developed to overcome this dilemma, one of which is the Delphi process. The Delphi technique⁶ (see [Figure 1](#)) is an interactive forecasting method using a panel of experts that answer a questionnaire in several rounds. After each round, a coordinator(s) provides an anonymous summary of the experts' ranking and comments; experts are encouraged to revise



their earlier answers in light of the replies of other members of their panel.

Delphi methodology has been used in the biomedical area for many years, for example, for the determination of best treatment options⁷. More recently, this technique has been used in the field of education to produce consensus competence frameworks for healthcare professionals, such as nurses⁸ and medical doctors⁹.

The way in which Delphi technology was applied in the present project is shown in **Figure 1**. In stages 1 through 3, a small expert panel consisting of the authors of this paper produced a proposal for a competence framework, starting with an initial Delphi round 1 framework produced by Brian Gennery and Patrick Crowley. The third and final version of this framework contained 46 proposals for competences in 13 categories (see **Appendix 1**). This proposal for a competence framework was then evaluated by a large expert panel consisting of industrial employees that are members of the EIPG, the EFPIA, the EUFEPS and/or other organisations, such as the Innovative Medicines Initiative¹⁰, and academics, members of the EAFP, between 10 July 2014 and 18 October 2014.

The large expert panel was invited via the internet (using *surveymonkey*¹¹) to rank and comment upon the 46 proposed competences (**Appendix 1**) using the uni-dimensional Likert method¹² with a scale of 1 to 4. Thus competences were ranked by giving a score of importance from 1 (lowest) through 4 (highest). Members of the expert panels also had the possibility to check a "I am unable to rank this premise" box. There was also the possibility of skipping a competence by not replying at all (blank). The "unable to rank" and blanks were summed.

The results presented here are those of the large expert panel consisting of industrial employees working in a biotechnological environment (n = 82); results are also

1. INITIAL QUESTIONNAIRE	<ul style="list-style-type: none"> production by small expert panel (authors of this article) a starting point to be modified in 3 consecutive rounds
2. EVALUATION BY SMALL EXPERT PANEL	<ul style="list-style-type: none"> small expert panel: authors of this article panel provide (1) rankings, (2) comments (what is unclear, missing, in duplicate, etc.)
3. MODIFIED QUESTIONNAIRE	<ul style="list-style-type: none"> production of modified questionnaire based on rankings and comments of small expert panel in 3 rounds 4th version for evaluation by large expert panel: 46 propositions for competences grouped into 13 categories
4. EVALUATION BY LARGE EXPERT PANEL	<ul style="list-style-type: none"> large expert panel: industrialists, academia, pharmacists from other areas of the profession panel provide rankings and comments

Figure 1: The Delphi technique as applied in the PHAR-IN project.

given for the total survey population (n = 257) that included, besides industrial employees working in a biotechnological environment, industrial employees not working in a biotechnological environment (n = 58), persons working in regulatory affairs (n = 50), hospital pharmacists (n = 32) and academics (n = 35).

Statistical analysis

Ranking scores for competences were compared using non-parametric methods. The statistical tests used are described on the GraphPad website¹³. For descriptive purposes, results are expressed as means. Medians were compared to the global median using the Wilcoxon signed rank test.

Comments were not analysed statistically.

Results

Survey characteristics

Participants came from all European countries, the main delegation being from the UK (16%) followed by Portugal (12%). There were 300 entries into the *surveymonkey* questionnaire, of which 43 (14%) were invalid (grossly incomplete and/or duplicates). Of the 257 participants, 54% were industrial employees (n = 140), 32% pharmacists from other areas of the profession (n = 82) and 14% academics (n = 35). Amongst the industrial employees and other professions, 25% worked in

regulatory affairs, 22% in research and development, 8% in production, 3% in marketing and 41% in diverse other occupations, such as quality assurance (31/140 industrial employees) and hospital pharmacy (32/82 other professions).

Of industrial employees, 36% worked in a small or medium enterprise, 35% in big pharma and 29% in other organisations. A total of 32% worked in a biotechnological environment (82/257). Some 76% of participants had a pharmacy degree, 20% a science degree and 4% a medical degree. Pharmacists formed the largest contingency of industrial employees working in a biotechnological environment (57/82 = 69.6%), 23/82 = 28.0% had a science degree, and 2/82 = 2.4% had a degree in medicine. Several participants stated that they would prefer to have a biotechnology course in the later stages of their primary degree (63%) and 37% as CPD. The bulk of the participants (82%) were aged between 31 and 60, the main age category (31%) being 41–50 years old.

Ranking of competences by industrial employees working in a biotechnological environment (n = 82)

The percentages of responses ranged from 76/82 = 96% (competence 1) through 55/82 = 67% (competence 19), the global response rate was 2986/3772 = 79%.



The highest percentages of those unable to score a competence ("I cannot rank this competence" or blank) were seen in categories 4 "Clinical pharmacology" and 12 "Ethics and drug safety". The means for competences from industrial employees working in a biotechnological environment (n = 82) are given in **Appendix 1**.

The highest medians were seen in category 1 and categories 6 through 11 concerned with research and development, product development, processing, and stability, respectively. Preclinical and clinical development, biological and advanced therapy, and ethics and drug safety scored low.

Ranking of competences by the total survey population (n = 257)

The global median was 3 and the global response rate $8862/11822 = 75\%$. As with ranking of competences by industrial employees working in a biotechnological environment, the highest means were for competences 1, 25–28, 30, 32, 33 and 39.

Comments

There were 59 comments made out of a possible total of (13 questions x 257 participants =) 3,341 (only 1.7%). Comments were made on the following.

1. The clarity of the survey, for example, regarding preclinical sciences "your question is not clear enough to provide an answer".
2. The context, for example, regarding research and development "I am not clear in what context you are asking these to be ranked".
3. The specificity to biotechnology, for example, regarding research and development "not really specific to biotech products".
4. The level in terms of foundation or specialist, for example, "I find the topics listed in each section to lack consistency in terms of 'general' and 'specialist'".

knowledge".

5. The balance between the relative importance of different areas, for example, regarding regulatory affairs "Fascinating that someone thinks there is more to discuss in regulation than in all other areas of development".

Discussion

Did the survey technique and the Delphi tool work satisfactory?

As $257/300 = 86\%$ successfully completed the survey, it appears that the survey was comprehensible on the whole. Of those completing the survey, response rates were high (all >55%) implying that those replying felt well-informed and able to give a reasoned answer. In some rare cases, response rate was low, e.g. for industrial employees working in a biotechnological environment for categories 4 "Clinical pharmacology" and 12 "Ethics and drug safety". This could be interpreted as meaning that the group had less experience of such matters and were less capable of replying in these areas.

The Delphi methodology requires that the survey be anonymous and so individuals or groups are not targeted. Thus, no limitations were fixed on the possibility to participate, and other professionals, such as persons working in regulatory affairs and hospital pharmacists, were recruited by snowballing. It is interesting that the ranking profiles of the total survey population were not significantly different from that of the industrial employees working in a biotechnological environment. Anonymity could be a (minor) issue in this study as Delphi requires complete anonymity. In the PHAR-IN study, the identities of the participants were known to the authors but not to each other. Albeit, one of the main precepts was maintained, viz that those surveyed were not selected. This avoids the possibility that the replies obtained find their origin in the competences of the experts chosen.

The number of participants is not

an issue. According to a 2012 survey by *Europabio*¹⁴, there were 52,540 employees in the European biotechnology industry. Using a confidence interval of 95% and a margin of error of 10%, the collected sample size equals 96. The sample size in this study was close to this figure: $82/96 = 85\%$.

Ranking of competences

Highest scores were attributed to six categories:

- Category 1 Research and development
- Category 6 "Upstream" and "downstream" processing
- Category 7 Product development and formulation
- Category 8 Aseptic processing
- Category 10 Product stability
- Category 11 Regulation.

This was true for biotechnological industrial employees and for the total population; it suggests that competences associated with the development and production of the product are specific to biotechnology.

Further papers will deal with other issues such as the statistical aspects of Delphi/Likert methodology, whether there is a difference between industrial employees and academics (educational providers), and between industrial employees and hospital pharmacists (users of biotechnological products), in what they think are essential competences for biotechnological practice.

Conclusions

On the basis of the scoring and the comments, the framework now needs to be refined in the areas of the following.

1. Balance: with development of some areas such as formulation, manufacture and quality control and diminution of the importance of issues non-specific to biotechnology such as preclinical pharmacology, reporting of AEs, critical review of published

- papers, and safety data in order to prepare a clinical trial plan. This will be of importance when proposing a framework for an undergraduate master course.
2. Clarity: with more thought given to possible misinterpretation of questions
 3. Context: with consideration of the stakeholders of the framework and related courses and a possible introduction of a two-tier framework (foundation and specialist)

If readers of this paper would like to participate in the PHAR-IN project, they are invited to visit the PHAR-IN webpage:
<http://www.phar-in.eu/>

Disclaimer

As the PHAR-IN project is funded by the EU, the courses and other elements are to be produced and used primarily in Europe.

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Appendix 1: The 46 proposed competences, divided into 13 categories, for practice in the biotechnological industry (n = number of competence)

n	Competences	Mean score
	1. Research and development	
1	Take an active role in a multidisciplinary team to interpret the key elements of a drug development strategy and use this to design early phase clinical studies	3.4
2	Understand the statistical principles used in preclinical and clinical research	2.9
3	Be able to critically review published studies in preclinical (including safety pharmacology) and clinical research	3.2
	2. Preclinical sciences	
4	Have an understanding of the choice and predictive value of the non-clinical testing programme as part of the overall drug development plan for chemical and biological compounds	3.2
5	Be able to describe the general principles of non-clinical safety testing	3.0
6	Know how non-clinical tests are integrated into the overall drug development plan (including scheduling of toxicology tests with respect to clinical trials)	3.2
7	Be able to use animal pharmacokinetics and toxicokinetics to inform the clinical development process	2.6
8	Describe the importance of the selection of the preclinical animal model in order to have a better and more predictive non-clinical phase	2.8
	3. Biological and advanced therapy	
9	Describe the breadth of advanced therapy medicinal products (ATMPs) that are available and in development, including the scientific principles for the classification into the categories of gene therapy, somatic cell therapy, tissue engineering and combined ATMPs	3.0
10	Describe the range of products available with recombinant DNA technology	2.9
11	Discuss the different needs between the preclinical and clinical trial needs of natural proteins and modified proteins	2.9
12	Describe the range of monoclonal antibodies available and those in development and discuss the potential long-term safety issues with monoclonal antibodies	3.1
13	Describe the global need for new and improved vaccines and the barriers to their development	3.0
14	Define what a therapeutic vaccine is and describe how a therapeutic vaccine could influence therapy in a common disease area	2.9
15	Describe what is a polysaccharide product and the regulatory and development challenges involved	2.8
	4. Clinical pharmacology	
16	Take an active role in a multidisciplinary team to design clinical pharmacology studies	3.0
17	Recognise the particular ethical issues of using non patient volunteers in clinical studies	3.0
18	Understand and interpret clinical pharmacodynamic and pharmacokinetic data especially that related to safety issues	3.2
19	Discuss how data from a clinical pharmacology study can inform the future development of a medicine	3.3
	5. Clinical development	
20	Use preclinical pharmacology and safety data to prepare a clinical trial plan	3.0
21	Write a protocol for a study including the choice of design, the end points, whether to use a placebo and the inclusion and exclusion criteria	2.9
22	Interpret the elements of good clinical practice that apply to the design and execution of clinical trials	3.2
	6. "Upstream" and "downstream" processing	
23	Understand "upstream" aspects of biopharmaceutical process development, such as cell line development and generation and characterisation of Master Cell Banks and Working Cell Banks, cell culture and harvesting	3.3
24	Understand "downstream" aspects of biopharmaceutical process development, such as isolation and purification of proteins	3.3
25	Identify Critical Quality Attributes and Critical Process Parameters and define a meaningful set of in-process controls and specifications to ensure quality and	3.3

26	Have good working knowledge of the principles of “comparability” as applicable to biopharmaceutical manufacturing changes	3.5
	7. Product development and formulation	
27	Understand the importance of defined quality standards for product and process components used in biopharmaceutical formulation and manufacture, and the potential for interaction with biopharmaceutical macromolecules	3.4
	8. Aseptic processing	
28	Understand microbiological principles as they apply to sterility assurance in biopharmaceutical manufacturing	3.3
29	Understand unit operations in aseptic processing and design of facilities and utilities in a sterile manufacturing suite	3.2
30	Understand concepts of good manufacturing practice and good distribution practice as applicable to the aseptic production, control, storage and handling of biopharmaceuticals	3.4
	9. Analytical methodology	
31	Understand the principles, instrumentation and application of analytical methods (especially bioassay) used to characterise biopharmaceutical raw materials, intermediates and finished products	3.2
	10. Product stability	
32	Understand the potential impact of environmental factors (such as temperature, light, oxidation) on biopharmaceutical proteins and consequences for product quality, safety and efficacy	3.5
	11. Regulation	
33	Understand the regulatory framework applicable to the development, manufacture, quality assurance and testing of biopharmaceutical products	3.6
34	Use research skills to find regulatory documents used for the preparation of a Clinical Trial Application	2.8
35	Use knowledge of specific legislation for biopharmaceuticals to review preclinical and clinical parts of a Marketing Authorisation dossier	2.9
36	Make decisions based on regulatory and commercial information about what text should be included in a Summary of Product Characteristics and Patient Information for a biopharmaceutical	3.2
37	Know how national agencies conduct GXP inspections and how to prepare for them	3.2
38	Have an appreciation of post-licensing responsibilities for drug safety and how to construct a risk management plan	3.1
39	Understand the life-cycle management of biopharmaceuticals	3.3
40	Understand the current regulatory requirements for biosimilars	3.1
	12. Ethics and drug safety	
41	Analyse and report adverse event data from clinical trials	3.0
42	Employ pharmaco-epidemiology skills, including the statistical methodologies to strategically evaluate a drug product and produce a risk management plan	2.6
43	Interpret clinical trial designs that address specific ethical issues, e.g. in special patient populations	2.7
44	Design a consent process that ensures that subjects are not coerced into participating in clinical trials	2.5
45	Utilise their knowledge to ensure that patient safety and patient education are priorities when either an originator biological molecule or a biosimilar molecule is dispensed in practice	3.0
	13. Commercialisation	
46	Understand the significance of biomarkers as an integral part of the development process and economic evaluation of biopharmaceuticals	3.1
Competences are given as means for descriptive purposes only Bold: competence median significantly higher than the global median of 3 (n = 2926) (Wilcoxon signed rank test)		