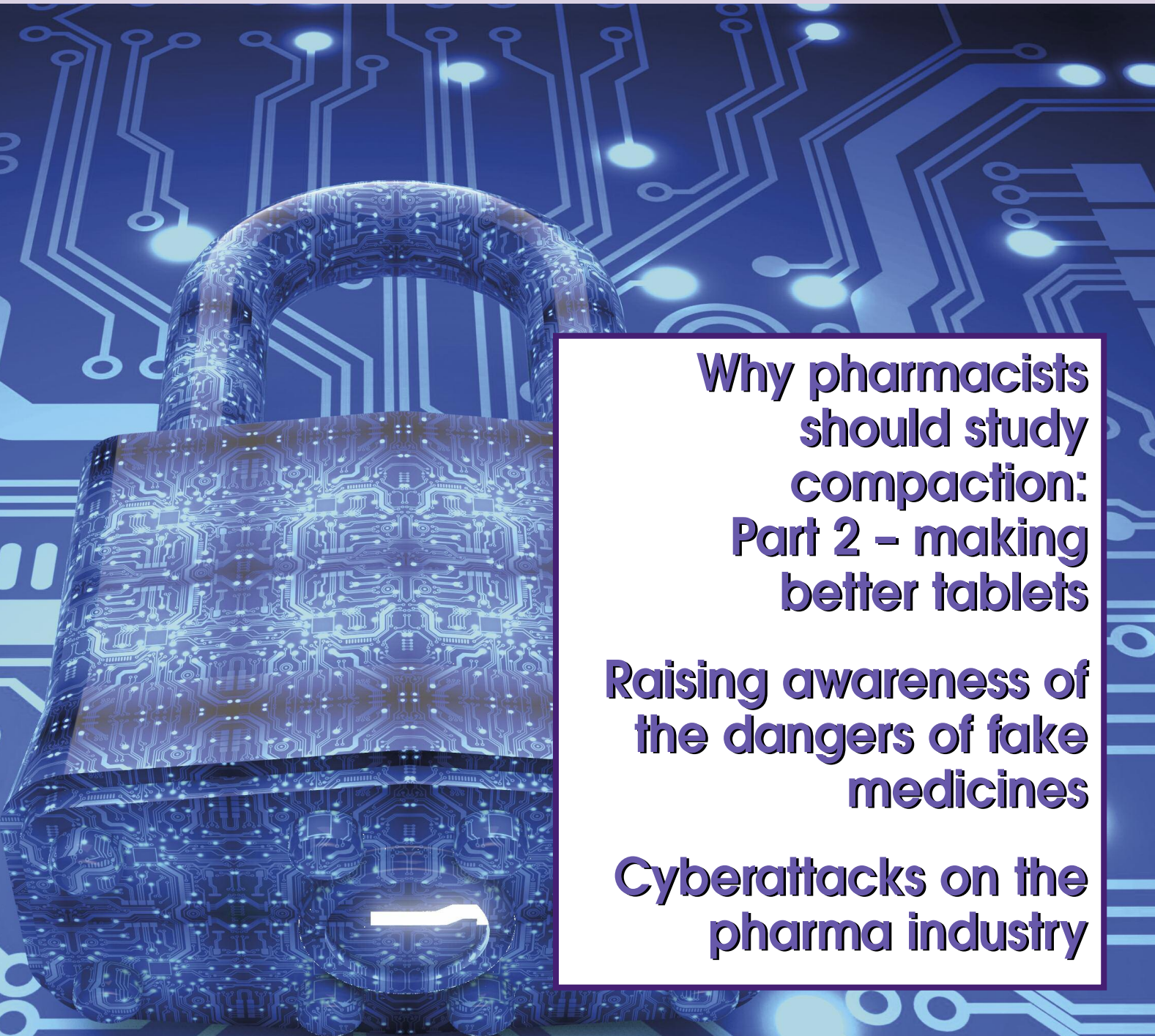


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**Why pharmacists
should study
compaction:
Part 2 - making
better tablets**

**Raising awareness of
the dangers of fake
medicines**

**Cyberattacks on the
pharma industry**

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Newton's laws, Einstein's theory or just plain science?

Time is running out fast. It may not seem that way – after all, we started with just over 1000 days between the publication of the Delegated Regulation governing the details of the safety features, and there are still about 600 days to go. However, advice issued by both the European Medicines Verification Organisation (EMVO) and the blueprint providers indicate that in any national system at least 6 months of testing with all users connected to the system are recommended, which means that for any country behind schedule, there are approximately 400 days – just over a year – left to get all systems on line for a testing phase.

Once again, the progress report issued by EMVO makes for sombre reading – only seven countries have signed a contract with the service provider and almost two-thirds of countries are behind schedule – which means that the blueprint providers will be faced with a number of national systems requiring commissioning, and the hub of the same systems coming on line *en masse*, close to the deadline, instead of in an ideally gradual manner. The irony – if not outright concern – is that the countries that are ahead of schedule or mainstream, for the most part, are countries with lower percentage losses in sales due to intellectual property infringement, according to the figures of the EU Intellectual Property Office, whilst at least half of the cohort of countries who are behind schedule rank in the top third of countries suffering from these losses, and which, therefore, seem to be most at risk – at least in relative terms in the European territory – of the presence of counterfeit medicines products in their pharmaceutical supply chain.

Clearly, an impetus is needed – if nothing else



to address lacunae in knowledge about how the entire system will operate once it is fully operational. It would probably be amiss to believe that, in Newtonian fashion, greater efforts will lead to a proportionately greater speed towards the objective. There are so many consequences arising from the regulation, many related to professional practice as well as technical implementation, that progress appears to be Einsteinian in nature – the progressive increase in the size of the challenge makes every extra amount of energy put into achieving the

objective appear less effective at actually moving faster towards the goal.

Yet, just as scientists continue to pour their efforts into overcoming the limitations of Einstein's theory, so must the world of pharma continue to reach for the ultimate aim of protecting all patients from counterfeit medicines. Relative amounts of counterfeit medicines in the EU compared to extra-European markets are of little comfort as long as the patient in every box is at risk. Moreover, just as scientists believe that the universal nature of their work is the key to their eventual success, so must the world of pharma remove all barriers to the universal participation of any pharmaceutical association – trade or professional – in this project. It is only through the active participation of all such associations that the project can hope to achieve the level of success that the investment of finance, time and effort demands.

A handwritten signature in black ink, appearing to read 'C. Farrugia', written over a horizontal line.

Professor Claude Farrugia
President, EIPG

WHY PHARMACISTS SHOULD STUDY COMPACTION: PART 2 – MAKING BETTER TABLETS

by Michael Gamlen

Helping people make better tablets is an interesting challenge – and the challenges are not only scientific! In this article, a new approach to tablet characterisation is described which has been shown to reduce development times and improve product quality. Using the latest technology, it is possible to check the compaction and lubrication properties of tablet formulation during routine quality control testing.

Michael Gamlen studied for a PhD with Professor JM Newton at Nottingham University and was Head of Solid Dosage Form Development at the Wellcome Foundation Ltd for 15 years. He is the inventor of the Gamlen Powder Compaction Analysis System, and works as a consultant and trainer. He is a regular contributor of articles on tableting and powder compaction.

Improving tablet quality by understanding the compaction process is becoming a reality. I recently visited India to demonstrate for our compaction analysis system to possible purchasers. The system includes two pieces of kit, the compaction analyser and the tensile tester, which travel in flight cases well within the airlines weight limits. I was travelling with our agent who had an extensive tour planned for us – three cities in 3 days, five client visits in all. In addition to the key instruments, I also carried a powder pipette – a small dispensing instrument which dispenses a fixed volume of powder and removes the need for sample weighing during the demonstrations. Travel in India is always interesting (challenging!) especially at busy domestic airports. Security were not often interested in the instrument itself but found the powder pipette, which is vaguely gun-shaped, a great challenge.

Our agent GS had visited us in London prior to the visit to get more information on the system, which set me the challenge of how to quickly demonstrate to him the impact of material properties on compaction behaviour. He has a technical

background but no direct experience of tableting. In the past, we have used a small roller system, marketed for grinding small stones, as a roller mixer to demonstrate the impact of material properties on mixing behaviour. I decided that we would use this to demonstrate the impact of lubrication on tablet properties, using two lubricants and two blending times. Using magnesium stearate as a “control” (?worst case material), and sodium stearyl fumarate – my preferred lubricant, I planned to do a simple comparison of 5 and 10 minutes blend on the compaction properties of a direct compression excipient.

Audience participation is a great way to get people interested, so while I used the powder pipette to dispense fixed amounts of powder (about 70 mg for a 5 mm tablet) and make the tablets, GS measured the tablet fracture stress and charted the values. As we were doing a simple comparison, we did not measure tablet thickness or weight; the pipette keeps the weight fixed and the thickness did not vary a great deal in the compaction pressure range of 80–180 MPa (200–500kg) which we were studying. We

collected compaction and breaking strength data on the four samples in less than an hour, and were able to see that whereas magnesium stearate reduced tablet strength after 10 minutes blending, sodium stearyl fumarate showed no effect of blending time – and made better tablets.

When we arrived for our first presentation in India, it was clear that the time available was not going to permit even a short evaluation of processing. The client had two samples from product batches made from two different batch sizes and which had given different results. They wanted to know if we could see the cause of the difference in behaviour. Again, we used the audience to assist with data measurement and recording. We prepared just one tablet at each of five forces from the two samples and got virtually identical results. This is not what the client wanted to hear! But actually, knowing that the process has produced the same material on two different scales was an important result. It showed that the observed differences resulted from the operating conditions of the tableting system and not the blend manufacturing process. It also showed that the compressibility of the formulations was marginal, and that increasing the compaction force did not result in increased tablet breaking strength. This is the sure sign of a risky formulation as the operator is likely to increase the compaction force to get a “better” tablet and instead cause capping – as happened here.

Another client visit stretched my data handling skills, to produce an easier way to visualise our compaction data. Our system uniquely measures both the compressibility and the lubricity of a product. We assess the compressibility through the measurements listed in Part 1 of this series¹ – plots of tableability, compressibility and compactibility. The target value for tableability (compaction pressure versus tablet tensile fracture stress) is a strength of 2 MPa at a pressure of 200 MPa. This has been accepted by most of the pharma majors as a desirable value,



with a lower fracture stress limit of around 1 MPa at the same pressure. The relative density of the product is targeted at 90% or less, although actual values up to 95% are not uncommon. The risk of high density formulations is over-compaction and capping. Lubricity is assessed by calculation of ejection and detachment stresses. Ejection stress should not exceed 5 MPa. There is no agreed standard for detachment (take-off) stress but we recommend a similar limit as for ejection.

I was very pleased to discover that

it is possible to generate gradient backgrounds in Excel charts which can be two (or more) colours, and turned at an angle while going through the origin. The results can be seen in **Figures 1–3**. Plot lines which lie in the green zone are acceptable whereas plot lines in the pink/red zone are high risk. As you might expect, there is significant blurring between the boundaries as these factors are not clear cut.

We decided to use this approach in the evaluation of direct compression product targeting the

orally dispersed tablets market. A well-validated approach to evaluation of direct compression materials, developed by my friends Colin Minchom and Tony Armstrong, is to measure the effect of adding progressively more of a test material to the direct compression system and measuring the effect on tableability (see above).

Using our powder compaction system, we were able to check the compaction and lubricity profiles of four levels (5, 10, 20 and 40%) of poorly compressible material (ascorbic acid) modelling a drug substance. As expected, the excipient system itself was highly compressible, and well lubricated (with sodium stearyl fumarate!). The tablet tensile fracture stress at 200 MPa was around 6 MPa – so tableability was well in excess of that needed for a good product. We estimated the density of the product at around 90%, well within safe bounds, and the ejection and detachment stresses were well below 1 MPa – again highly desirable. As we added successively larger amounts of model drug, there was little effect on tableability except at the highest concentration (see **Figure 1**) and all the plot lines were well away from the pink danger zone. Ejection stress (**Figure 2**) showed some small increases with increasing levels of model drug, but remained well out of the 5 MPa danger zone. Detachment stress (**Figure 3**) showed similar changes to the ejection stress and again were well within limits. When we presented the data to the excipient manufacturer, they were very pleasantly surprised both with the quality of the data, and the speed of generation. They quickly realised the technique's potential value.

Compaction studies based around tablet fracture are well-established having been developed in the 1950s. Their major limitation is that for them to work, you need to make, eject and break a tablet. If you have a material which does not make a tablet or is not lubricated, then the "make and break" approach cannot be used. In this situation, what is

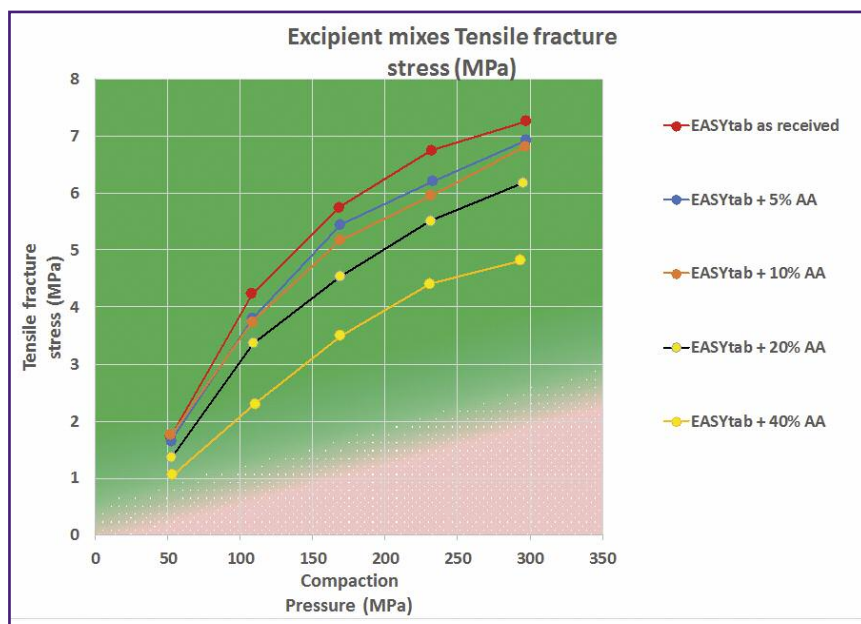


Figure 1. Excipient mixes Tensile fracture stress (MPa).

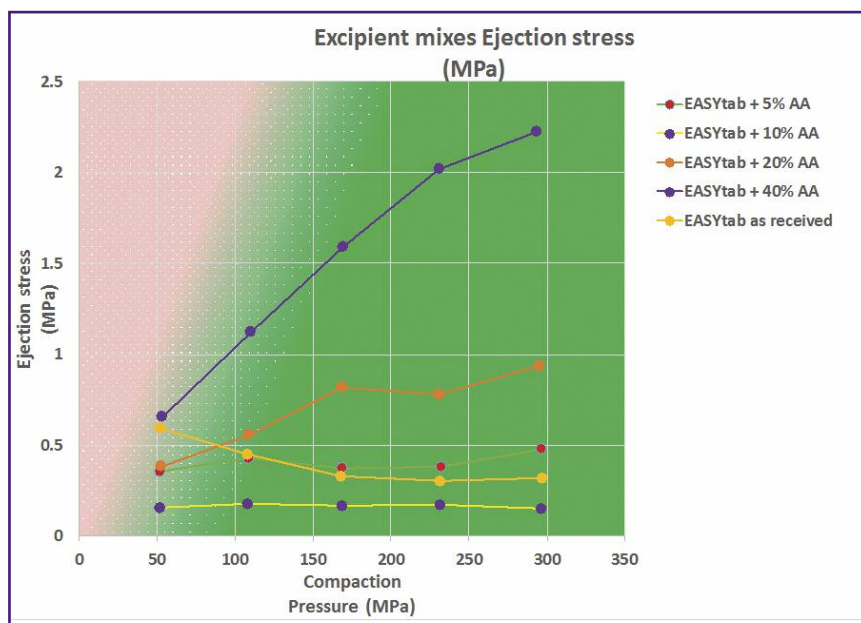


Figure 2. Excipient mixes Ejection stress.

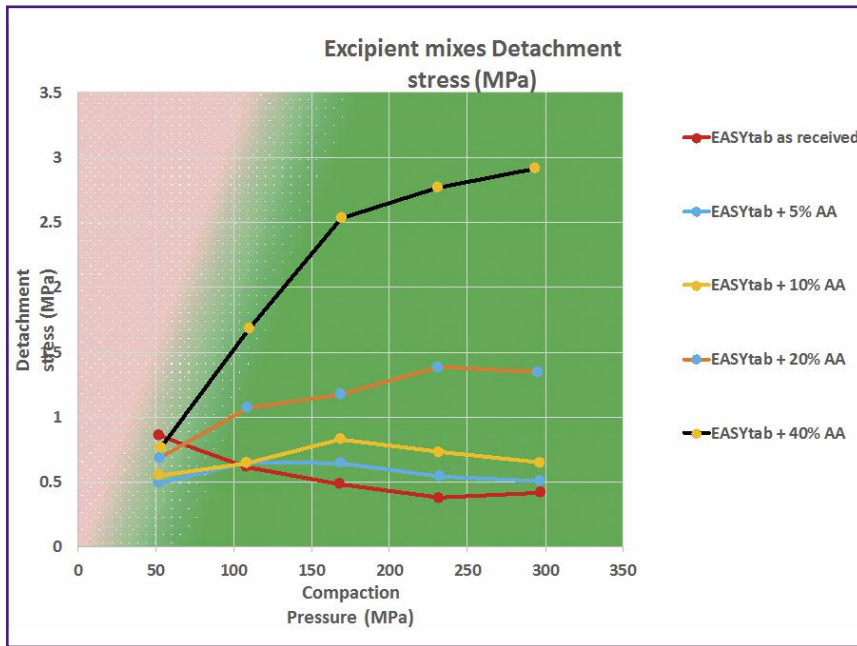


Figure 3. Excipient mixes Detachment stress.

needed is a system to evaluate the compaction process itself during the compaction event. This is known as compaction analysis – a method which has been widely used with studies going back to the 1930s. In my next article, I will discuss the utility and limitations of compaction analysis, the pitfalls and the problems, and how we might overcome them in the future.

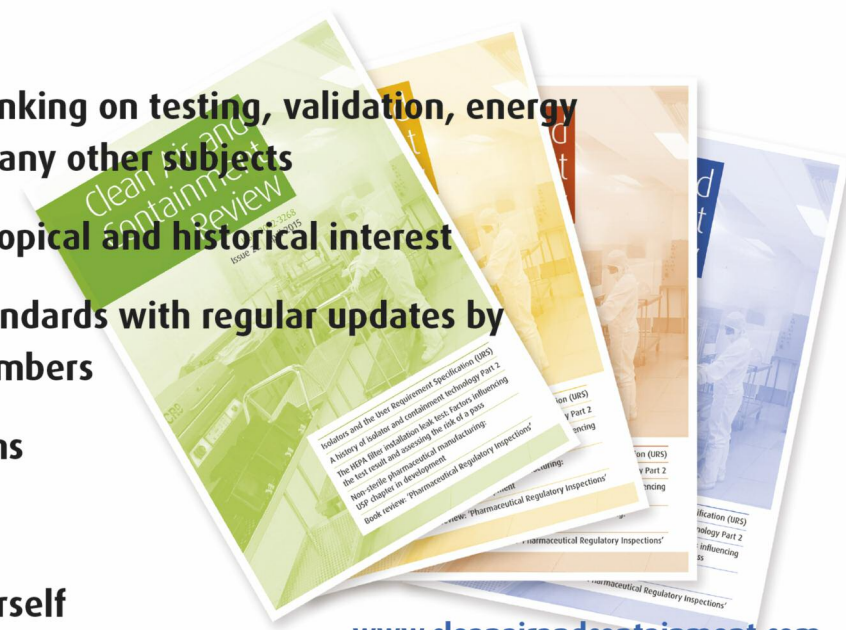
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RAISING AWARENESS OF THE DANGERS OF FAKE MEDICINES: THE MAKING OF A WORLD HEALTH PROFESSIONS ALLIANCE VIDEO

by Lin-Nam Wang

Ten billion euros is the figure estimated to be lost by pharma each year due to fake medicines, according to a report from the European Union Intellectual Property Office (EUIPO) in 2016¹. This, the EUIPO says, corresponds to 4.4% of the industry's sales, which translates into direct employment losses of around 38,000 jobs. But the cost to health and human life is far, far greater. In 2016, the World Health Professions Alliance (WHPA), as part of its long-term work against fake medicines, released a video "Counter the Counterfeits". This article shares how this project — led by the International Pharmaceutical Federation (FIP) — came to fruition.

Lin-Nam Wang is a pharmacist and communications manager at the International Pharmaceutical Federation.

Disability and death

Interpol estimates that a million people are killed by fake medicines each year². Of these deaths, around 12% are caused by people taking fake antimalarials in Africa, where almost a third of these products are counterfeit³. Citizens of developed countries have also been affected, with casualties including 149 killed by fake heparin in 2007/08 in the USA, for example⁴. Permanent disability, prolonged illness, spread of disease and resistance to treatment add to the harm that counterfeit medicines inflict on our societies. What is particularly repugnant about this criminal activity is that people are being hurt by something they take in the belief that it will help them. Moreover, it is the most vulnerable in our societies — the sick and the poor — who tend to be most at risk.

Despite the police raids that seize

millions of dollars' worth of these potentially deadly products and moves to roll out anticounterfeiting measures, such as track and trace, the problem of fake medicines appears to be growing. The internet has made it all too easy for fake and substandard medicines to reach consumers. In some countries, fake medicines continue to be sold by hawkers in markets, at road sides and even on buses. That some medicines are prohibitively expensive and, in some cases, a consumer preference for anonymous purchases only serves to exacerbate the situation.

Deep concern

It should come as no surprise that healthcare professionals are deeply concerned about fake medicines. For a number of years, the WHPA, which gathers together global federations of pharmacists, nurses,

doctors, dentists and physical therapists, has been advocating for more action as part of its mission to improve global health and patient safety.

Surveys in Europe, Asia and the USA indicate that the general public have low awareness of the existence of fake medicines and their associated risks⁵⁻⁷. It is clear that improved education and awareness are part of the solution.

The WHPA's work has included making grants to countries to run national counterfeit medicines awareness projects and producing a handbook for health professionals entitled "All you need to know about spurious medicines"⁸. Most recently, however, it resolved to broaden the scope of its campaign, aiming to gain a more international reach, and deliver messages to three target audiences: the public, health professionals and policymakers. But how?

A new project

It was clear that making a video could be an answer. Video has become a key communications tool in education and marketing, allowing information to be spread throughout the world in a matter of seconds and to any number of devices. People are watching more and reading less. Moreover, humans are audio-visual creatures and video, by engaging the senses of sound and sight, makes more of an impact. But the established popularity of video as a communications channel also meant that, undoubtedly, there would already be a number of videos raising awareness of the dangers of fake medicines.

A review of what was available on the internet confirmed this, showing at least 17 existing videos on the topic, albeit with mixed results in terms of viewing numbers on their corresponding social media channels — anything from double digits to a couple of hundred thousand. Notably, and as you may expect, the videos that were the most successful were the ones with an element of shock value or risqué humour. For example, a 2009 production by the UK's Medicines and Healthcare Products Regulatory Agency and



Pfizer featuring a man regurgitating a dead rat had over 100,000 YouTube views at the end of 2015, and a video from the Federal Union of German Associations of Pharmacists in 2008, entitled “Big Dick sells Viagra” had over 200,000 YouTube views.

The question was how the WHPA project could bring something a bit different to the table so as to ensure the best use of a relatively small budget. A brainstorming session led to the idea of exploiting a function of YouTube to incorporate interactivity into the video. We wanted to confront the viewer with a situation to which relatively little thought is often given — buying a medicine — and to send home the message that there is a need to think twice about the choices he or she makes. At this stage, we decided that we wanted a split screen video showing two scenarios and asking the viewer to choose between two products (see **Figure 1**).

Preparation and action

One of the most vital stages in the project was to write a good brief, incorporating the key messages we wanted to give to each target group and communicating that fake medicines pose a universal threat to people in all countries and of all ages. It was important to clarify our aims. We wanted to warn people, in general, of the risks of fake medicines and help them to avoid the harms that they could cause. At the same time, we wanted to provide guidance to health professionals on how to avoid becoming inadvertent suppliers of fake medicines and what to do if a patient suspects that he or she has taken a fake. We also wanted to call on policymakers to take greater action on this issue.

A fundamental step was to draft a script that included all these messages, approved by each of the WHPA partners (see **Figure 2**). This, along with the brief, was given to the video production companies tendering for the project, for their input. From the tenders and

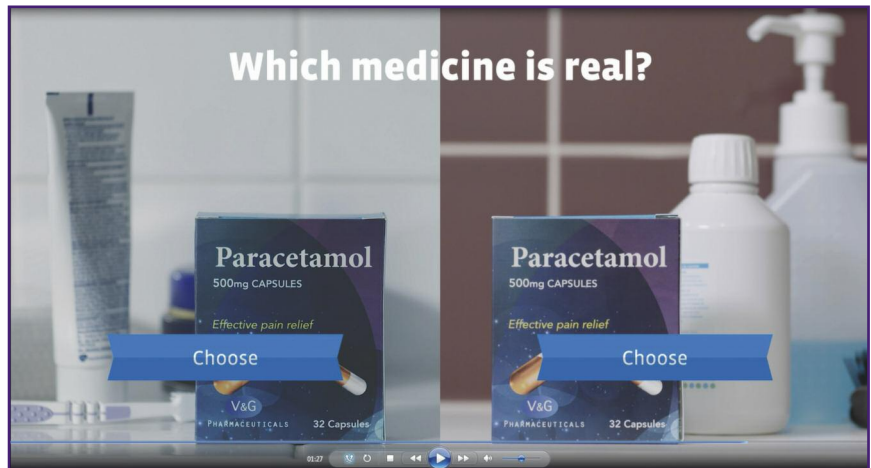


Figure 1. Asking the viewer to choose between two products.

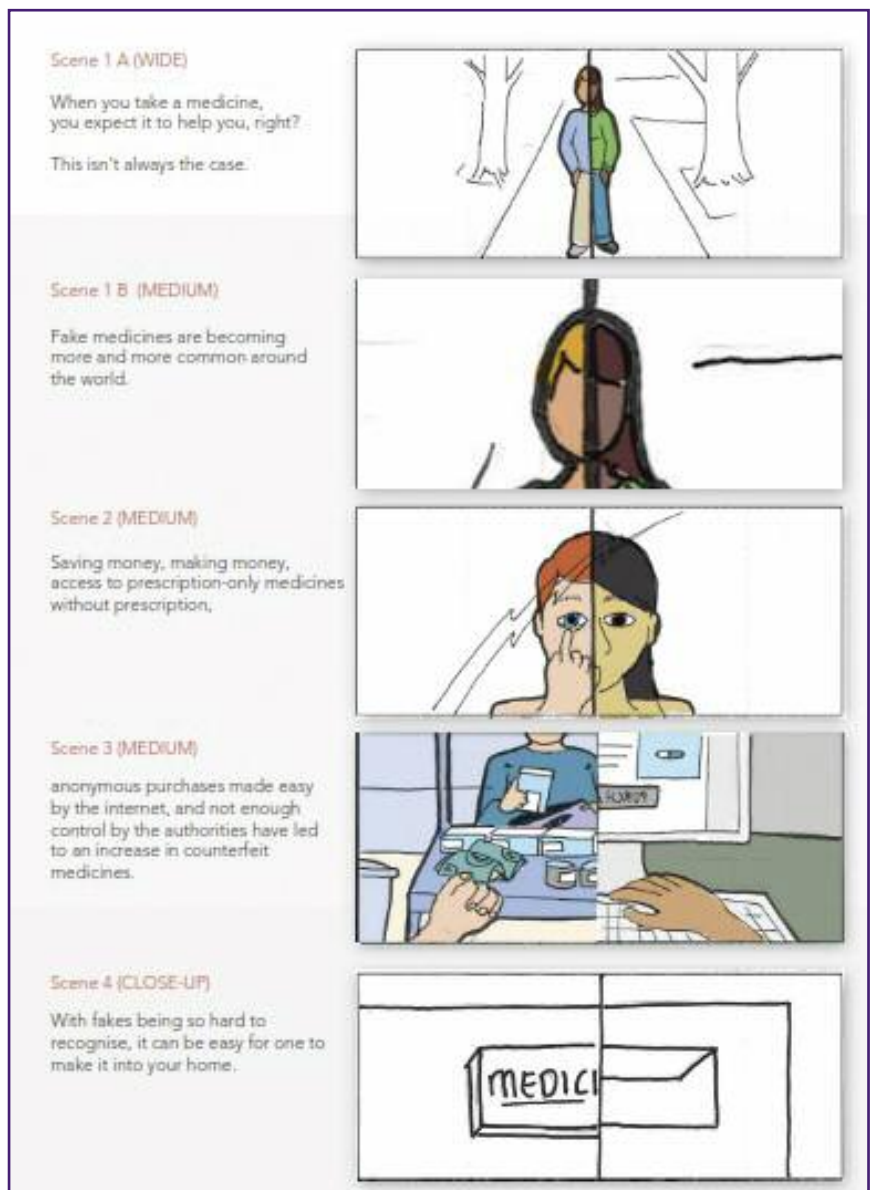


Figure 2. Storyboard sketch of the video content.

proposals received within the budget, it was decided that, since all three target groups were, essentially, consumers, a single video would be



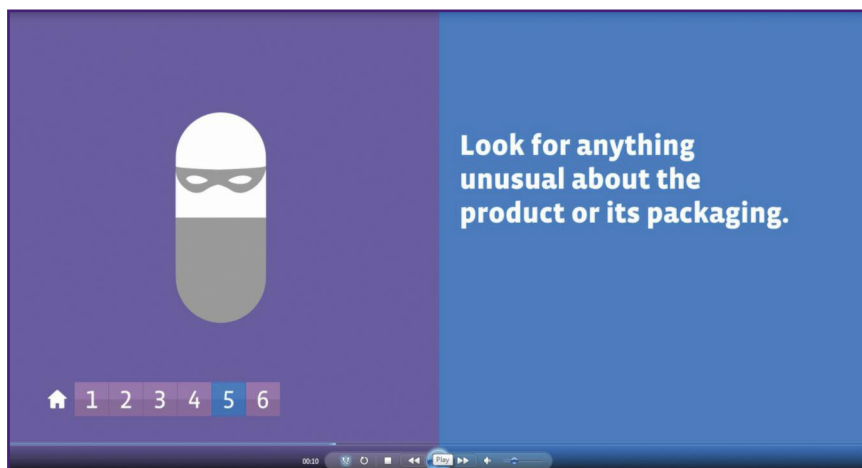


Figure 3. Animated guidance measures within the video.

exercise. FIP and production company staff and friends volunteered to take part so as to feature people of as many races and ages as possible throughout each of the 24 scenes. Accuracy, authenticity and the need to avoid identifiable brands were also high on the list of priorities. Mock but realistic packs of medicines were produced as props, as well as a mock-up online medicines retail website. We also made full use of our pharmacy contacts to provide generic looking tablets and to allow filming to take place in a hospital.

produced, accompanied by three further, more targeted parts.

Tone and style were a careful consideration. We thought that to better communicate that the risks of fake medicines are real, actors rather than animated characters, for instance, should be used for the first video despite the higher associated production costs. The three further parts, containing guidance for each target group broken down into five or six avoidance “measures”, were animated (see Figure 3). Table 1 shows the measures for consumers and Table 2 shows the measures for healthcare professionals.

Wanting an international reach also brought up a question of languages in addition to English. French, Spanish and Arabic were considered as priority languages for translation, which could be provided with little cost through the WHPA network.

It was also important, at an early stage, to have a communications plan in place for disseminating the video as widely as possible once it was made. Potential distribution channels were listed and included the WHPA and its partners’ websites, publications, social media accounts and press contacts, national member organisations of the WHPA partners, other campaigners against fake medicines and governments.

The filming of the video took 2 days and, because of a relatively small budget for what we wanted to achieve, it was an all-hands-on-deck

Tell your healthcare professional if a medicine has no effect or an unexpected effect. If you suspect you’ve taken a fake, seek help immediately. But don’t panic and don’t stop all your medicines.
Only buy medicines from authorised sources. Check with your health authority or national pharmacy organisation whether a supplier is authorised. Never buy medicines at the roadside.
If you buy online, be sure to use an authorised pharmacy. For example, check with your country’s pharmacy organisation. In the EU, you can look for and click on the European Commission online pharmacies logo.
When you travel, consider taking any medicines you might need with you. Keep in mind that you cannot be sure of safety in unfamiliar circumstances.
Look for anything unusual about the product or its packaging. If you think a medicine is fake, report it to a healthcare professional.
Remain alert to the risks of fake medicines. Share these tips with your family and friends.

Table 1. Measures consumers can take to avoid the harm of fake medicines.

Educate your communities on unsafe sources, what to look for (e.g. intact packaging, properly sealed, clearly labelled with dosing, manufacturer, batch number and expiry date), and what to do if they think a medicine is fake. Lobby your politicians to involve them in combating counterfeits.
Keep the legitimate supply chain secure by only sourcing medicine from authorised sellers. Be suspicious if you are offered a medicine at an unusually low price (especially from a new source).
Inspect your products. Know what to look for. A checklist to help you carry out visual inspections of medicines is available at: www.fip.org/ctc . For example, have tablets/capsules changed in size, shape, colour or odour? Be ready to adopt new practices and technologies to combat counterfeiting.
When supplying a medicine, tell patients about the expected effects and side effects, including time-span. Tell them to come back to you if the medicine has no effect or an unexpected effect.
If someone thinks they have a fake medicine, act quickly to give health advice, including on emergency care and therapy reassessment. Establish the source of supply, if the medicine has been taken and how much, and if there have been any adverse effects.
If a product is suspected to be fake, warn colleagues and notify the official manufacturer. Comply with the instructions of your drug authority (which may include patient tracing and product recall). Act to avoid disruption of treatment and give balanced information.

Table 2. Measures healthcare professionals can take to prevent the harm of fake medicines.

How did we do?

The video and animations, which were released in September 2016, can be seen at www.youtube.com/watch?v=aEJd0T7Nhf4, or scan the QR code below.



The storyline leads to the viewer being asked to choose between two products and being shown the consequence of their decision: depending on his or her choice, either recovery from an illness or admission to hospital.

Since its launch, the video has had over 168,000 views and reached over 847,000 people on FIP's social media alone. Enthusiasm for the video was expressed by the World Health Organization and government agencies. The Icelandic Medicines Agency, for example, asked for permission to use it and the video has been shown on a website jointly run by Austria's Ministry of Health, police and Chamber of Pharmacy. A specially produced standalone (non-interactive version) has been screened at conferences in China, Taiwan, Ghana, Zambia and Nigeria and outreach efforts led to media coverage in Europe, the Americas and Asia. The "Counter the Counterfeits" standalone video is free for anyone to use for non-commercial purposes and can be obtained by emailing fip@fip.org.

How else could we stop people being killed?

FIP views this project as a success. If it has prevented even one person from harm, then it has been a worthwhile use of resources. But the fight is far from over. Much more effort is needed if we are to stop the tragedy of people being injured or killed by fake medicines. We want policymakers, in particular, to do the following.

- Create strong laws or strengthen existing policies, such as making reporting mandatory.
- Ensure there are systems in place for rapid alerts.
- Make sure all stakeholders — police, customs and healthcare professionals and their associations — are involved and trained.
- Remain aware of sources of counterfeiting in legitimate and illegitimate supply chains.
- Allocate sufficient resources to protect the public through stronger enforcement.
- Make sure the health system has mechanisms, such as barcoding or radio-frequency identification tagging, in place to trace legitimate products.
- Seek technologies that help to protect the supply chain.
- Involve healthcare professionals in policy decisions and guidance so that these are appropriate for real-life settings and will be put into practice.
- Legislate for stronger penalties for counterfeiters.

FIP and the WHPA is continuing to work on the worrying issue of fake medicines, calling attention to the problem and advocating for solutions at all levels. More innovative solutions and more coordinated efforts are needed.

Acknowledgements

FIP is grateful to all those who supported the production of the "Counter the Counterfeits" video, including St Antonius Hospital in Nieuwegein, the Royal Dutch Pharmacists Association and Transvaal Pharmacy in The Hague; and, in particular, Mr Rob Moss, Mr Johan Oltvoort, Ms Judith Bijloos and Mr Paul Lebbink, as well as to all the volunteers who featured in it. We are also thankful for the support from our wide network of national

professional organisations, which helped to disseminate the video, and for an educational grant from Lilly, which went towards production costs.

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CYBERATTACKS ON THE PHARMA INDUSTRY

by Dr Nicola Davies

A cyberattack is defined as the “deliberate exploitation of computer systems, technology-dependent enterprises and networks”¹. In other words, it involves an intentional attempt by hackers to infiltrate and impair a computer network or system. Cyberattacks usually involve breach of access in terms of blocking user access and causing disruption of services. Such attacks can lead to cybercrime, which involves identity theft, data alteration, money theft, password loss, malware virus, and other malicious consequences¹.

Dr Nicola Davies is a psychologist and freelance writer with a special interest in the health and pharmaceutical industry. She has written for over 100 magazines in 10 countries. You can follow her work on Twitter (@healthpsychuk) or sign up to her free blog <https://healthpsychologyconsultancy.wordpress.com/>

No company, regardless of its type or size, is invulnerable against cyberattacks. In 2014, the three industries which had the highest threat for cybercrimes were aviation, chemical and pharmaceuticals². In 2015, a study showed that more than 66% of the pharmaceutical companies surveyed had a breach of access, whereas 25% were attacked by hackers³. In the case of pharmaceutical cyberattacks, the incentives are mainly financial, as the intellectual property (IP) associated with drug manufacturing are valuable. However, the attacks can also involve corporate spying; pharmaceutical and biotech companies contain diverse data, ranging from patient medical records to drug development and clinical trials results, information which is invaluable to competitor companies⁴.

Cyberattacks in pharma: why so easy?

Historically, pharmaceutical companies used isolated information technology (IT) systems that were not connected to the Internet, hence they were not designed for cyber security. However, digital health by means of

health tracking devices, big data analytics, remote access, patient data uploaded to the cloud, shared access with other organisations, and a general connection to external environments and the Internet, has led to the Internet of Things (IoT).

E-Health has allowed pharmaceutical companies to grow faster, to gain access to valuable data, to develop personalised drugs, and better communicate and engage with patients⁵. For instance, Novartis has signed an agreement with technological company Qualcomm to produce an inhaler which will connect to the Cloud and will promote Novartis' new drug for chronic obstructive pulmonary disease, Onbrez.

This type of health technology will allow patients and physicians to access patient's data and medical history at any time and by any device. Although this new health digitation produces many health and financial benefits, sensitive patient information becomes desirable for striving hackers and cybercriminals⁶. Through the Industrial Control Systems Supervisory Control and Data Acquisition (SCADA) networks, pharmaceutical companies can

connect to all types of external environments and access pertinent data and analytics. However, SCADA networks were inadequately designed against cyber threats⁷. The lack of security controls became obvious when a very maleficent attack, known as Dragonfly or Havex, a virus especially designed for pharmaceutical companies, allowed hackers to access, impair, and steal data from pharma IT databases⁸. Furthermore, the medical device is also not designed against cyberattacks. As Mr Valencia, Senior President of Qualcomm Life, states, “They [medical devices] weren't designed with the idea in mind that they would be going over the network and the information would be residing in cloud infrastructure.”⁸

In addition, patient data is scattered across many domains and shared with other organisations, hospitals and academic institutions. Therefore, a breach of access can occur at any time during the data sharing. Even if one pharmaceutical company has updated cyber security systems, there is no reassurance that the other organisations maintain the same level of security⁸. Indeed, based on a survey conducted by Ponemon Institute in 2016, only 16% of healthcare and pharmaceutical organisations perform routine checks and follow systematic monitoring processes against cyber threats. Furthermore, only 34% of the respondents reported that they have the necessary tools to perform cyber threat monitoring, whereas 29% indicated they have the resources to alleviate these threats. Finally, only 26% of the healthcare and pharmaceutical respondents asserted that they have the capabilities to examine and comprehend these threats⁹.

These findings emphasise the necessity for investing in cyber security and demonstrate the ease of breach of access within the chain of data sharing, as not all pharmaceutical companies are able to monitor and fight cyberattacks. In addition, pharmaceutical companies often merge with other



companies or are procured by more powerful brands. These companies have often suffered from hackers' attacks, as the confidential information regarding a merger or a procurement before becoming known can be used for profit in the stock market¹⁰.

The impact of cybercrime in pharmaceutical companies

One of the crucial aftermaths of cyberattacks in pharma is a loss of income, as IP and research and development (R&D) processes are highly costly. It has been estimated that the consequences of cybercrime costs the UK pharmaceutical industry at least £27 billion per year¹¹. Furthermore, in a global analysis survey of cybercrime, conducted by the Ponemon Institute and comprising 237 companies in six countries, it was calculated that the annual cost of cyberattacks for the pharmaceutical industry reached almost \$5 million in 2016 (see **Figure 1**)^{12,13}.

Theft of IP

IP constitutes the basis on which the R&D of new treatments and drugs is constructed. IP is vital in improving patient's lives, promoting innovation, increasing competitiveness, and consolidating the growth of the company. Biopharmaceutical IP involves patient data, drug patents, molecular formulae, production processes, and compliance data, among others¹³. It is estimated that the cost of developing a profitable drug can surpass \$2.6 billion per year, mainly due to technical, regulatory and financial challenges associated with R&D procedures¹⁴. IP embezzlement provides the cybercriminal and the improper competitor to bypass the risks and costs involved with R&D pipelines and directly develop an effective and successful drug¹⁵. In particular, there are three main data domains which are most valuable to hackers.

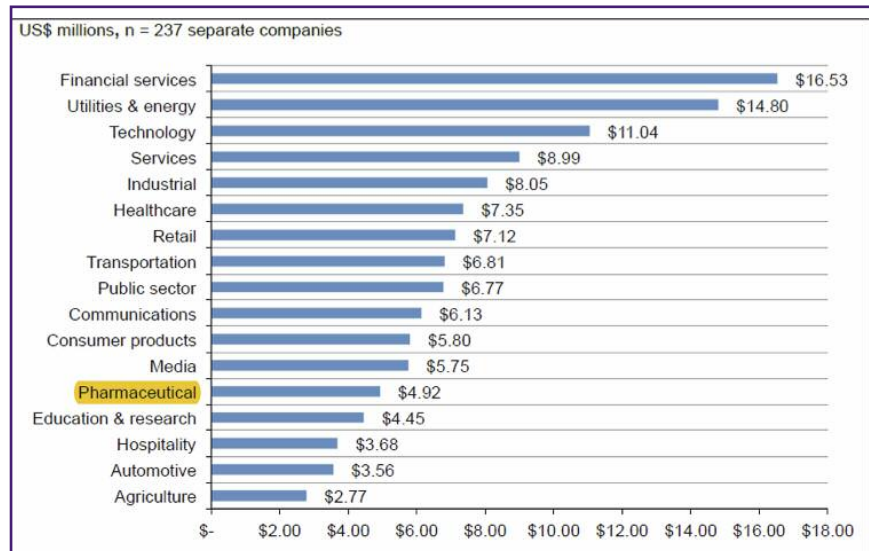


Figure 1. Average annualised cost by industry sector¹⁶.

- Clinical trial data, as this type of information is not only patient sensitive, but also provides commercial advantage.
- Company inside information and confidential data regarding drug development.
- Drug pricing policies and marketing strategies. This type of data offers an unfair advantage to the cybercriminal, as cleverly implemented market launch strategies are highly beneficial against strict healthcare budgets¹⁶.

Breach of access due to cyberattacks does not only result in data confidentiality issues (patients' medical data becomes known), but also in data integrity problems (patients' medical data becomes altered)¹⁶. Organisations, but also individuals, can pursue lawsuits on the grounds of negligence and breach of IP confidentiality. This implies costs for attorney fees, court cases, and also fines for lack of regulatory compliance¹⁷.

Sequential consequences

Breach of confidential data can also lead to prosecution, which not only harms the company financially, but can also damage its image and reputation. These cyberattacks hurt the prestige of pharmaceutical

companies, resulting in damaging customer relationships and marketing catastrophe. Rebuilding a company's reputation and gaining people's trust again requires significant spending on public relations and communication approach strategies¹⁷.

A cyberattack implies impairment or impediment of operations, constituting another economic burden related to cybercrime. Technical examinations are vital to identify faults in security controls, and investment in stringent and newer cyber security measures are also crucial; the implications associated with failing to employ these safeguards include further financial impact on the affected pharmaceutical companies¹⁸.

Litigations can also lead to pharma companies being required to re-run clinical trials. Besides the economic implications of designing and launching clinical trials again, the setback of timely access to essential medicine may be at the cost of human lives¹⁸.

What are the necessary steps to be taken against cyberattacks?

The cybercrime affecting the NHS and the various cyberattacks that have taken place in the last few years pose a real challenge for pharmaceutical companies. Fortunately, however, there are

some vital steps companies can take to protect their data.

1. **Apply more rigid access controls.** This measure involves authenticating users with the Risk-Based Authentications system, employing more difficult passwords, reducing privileged access and limiting access to unstructured data.
2. **Raise cyber security awareness.** This step relates to all IT staff employed by pharmaceutical companies, as they should be informed about the latest updates in security solutions and be able to report a potential malware infection and better identify dubious activities.
3. **Reassess security controls.** The outdated IT systems used by pharma need to be updated with new security controls against Internet threats, such as installing firewalls, extending risk assessments, and ensuring regular updates in security systems.
4. **Focus on data protection.** More emphasis must be placed on effective data encryption, especially when dealing with medical records and other sensitive patient data¹⁹.
5. **Invest in cyberattack prevention.** This includes data leak detection resources. Also, previous hacking attempts and attacks should be closely monitored as they can occur again.
6. **Create a cybercrime analytics programme.** This involves constructing a software programme which will not only scan for potential cyber threats but will also collect and analyse information on all hackers' crimes and present the results via meaningful data analytics¹⁹.
7. **Security via regulation.** The pharmaceutical industry is

one of the highest regulated sectors and needs to comply with various laws and procedures. The US Food and Drug Administration (FDA) 21 CFR Part 11 is one of the most relevant regulations, as it demands from the pharmaceutical companies to apply monitoring, reviewing of older documentations, electronic audit controls, and determining weak points in the security systems when dealing with electronic patient records. Thus, strict compliance to this FDA regulation will ultimately result in better cyber security¹⁹.

Cyberattacks are not random acts, but well-thought-out and thoroughly planned violations. Although the consequences are serious for all industries, for pharmaceutical companies they are potentially even more severe, as cybercrime can result in the endangerment of human lives. Regardless of whether the motives behind the cyberattacks are financial or strategic, these threats need to be monitored, scrutinised, and prevented. Investing in robust cybercrime security and raising awareness are essential measurements to be taken to avoid vulnerabilities, potential loss of income, and marketing catastrophe.

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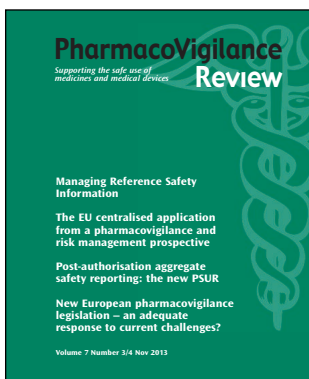


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regulatory review

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

Frequently asked questions (FAQs) - USA/European Union (EU) Mutual Recognition Agreement (MRA)

The US Food and Drug Administration (FDA) has published a very helpful set of 12 FAQs dated 2 March 2017 on the recently announced Decision No 1/2017 of the Joint Committee established under Article 14 of the Agreement on Mutual Recognition between the European Community and the United States of America, of 1 March 2017 amending the 1998 Sectoral Annex for Pharmaceutical Good Manufacturing Practices (GMPs), in particular its Article 14 and Article 21.

***Burkholderia cepacia* complex poses a contamination risk in non-sterile, water-based drug products**

The FDA advises drug manufacturers of non-sterile, water-based drug products that there have been recent product recalls due to *Burkholderia cepacia* complex (BCC) contamination. BCC and other water-borne opportunistic pathogens are among the contaminants that can be found in pharmaceutical water systems.

BCC survive or multiply in a variety of non-sterile and water-based products because it is resistant to certain preservatives and antimicrobial agents. Detecting BCC bacteria is also a challenge and requires validated testing methods that take into consideration the unique characteristics of different BCC strains.

People exposed to BCC are at an

increased risk for illness or infection, especially patients with compromised immune systems.

Specifically, the FDA is reminding drug manufacturers of six specific measures to take, with specific references to legal requirements for each as detailed in 21 CFR 211 and 21 CFR 314.

Modernising the way drugs are made: a transition to continuous manufacturing

Recent advances in manufacturing technology have prompted the pharmaceutical industry to consider moving away from batch manufacturing to a faster, more efficient process known as continuous manufacturing. The FDA is taking proactive steps to facilitate the drug industry's implementation of emerging technologies, including continuous manufacturing, to improve product quality and address many of the underlying causes of drug shortages and recalls.

The Center for Drug Evaluation and Research's Office of Pharmaceutical Quality Emerging Technology Program addresses not just continuous manufacturing technologies, but also other advances like 3D printing, novel dosage forms, and novel container systems. Under this program, the FDA engages with industry early in the process of developing new technology, and discusses any anticipated regulatory or scientific issues that may be part of a future application.

Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Living Donors of Human Cells, Tissues and Cellular and Tissue-Based Products (HCT/Ps) - Guidance for Industry

This guidance finalises the draft guidance dated December 2015 (80 FR. 77645). The finalised guidance provides establishments that make donor eligibility determinations for donors of HCT/Ps, with

recommendations for testing living donors for West Nile Virus (WNV) using an FDA-licensed donor screening test. The FDA believes that the use of an FDA-licensed nucleic acid test will reduce the risk of transmission of WNV from living donors of HCT/Ps and, therefore, recommends its use to test living donors of HCT/Ps for evidence of infection with WNV as set forth in this guidance. This guidance does not provide information regarding testing of cadaveric HCT/P donors for WNV.

Providing Regulatory Submissions in Electronic Format

The version of this guidance posted on 5 May 2015 provided a timetable of 24 months after issuance of the final guidance for the initial implementation of the electronic submission requirement for new drug applications (NDAs), abbreviated NDAs (ANDAs), biological licence applications (BLAs), and master files, and 36 months for commercial investigational new drugs (INDs). The timetable indicated that NDAs, BLAs, ANDAs and master files were to be submitted electronically in electronic common technical document (eCTD) format starting on 5 May 2017 (5 May 2018 for commercial INDs). The FDA has determined, in response to industry comments and internal review, that it is appropriate to extend the required date to submit master files in eCTD format by 1 year to 5 May 2018. Among other factors, the FDA recognises that there have been challenges with submission of master files in eCTD format, and eCTD uptake data for master files, in particular, indicated that adhering to the 5 May 2017 date could have led to high rejection rates of master files and thus slower FDA review processes, and, therefore, potential unnecessary delay in the review of some drug applications. This guidance has been revised to reflect this updated timetable.



Guidance for Industry - Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims

This final guidance is intended to assist applicants in developing labelling for cardiovascular outcome claims for drugs that are indicated to treat hypertension. With few exceptions, current labelling for antihypertensive drugs includes only the information that these drugs are indicated to reduce blood pressure; the labelling does not include information on the clinical benefits related to cardiovascular outcomes expected from such blood pressure reduction. However, blood pressure control is well established as beneficial in preventing serious cardiovascular events, and inadequate treatment of hypertension is acknowledged as a significant public health problem.

The FDA believes that the appropriate use of these drugs can be encouraged by making the connection between lower blood pressure and improved cardiovascular outcomes more explicit in labelling. This guidance recommends standard labelling for antihypertensive drugs except where differences in labelling are supported by clinical data. The FDA encourages applicants to submit labelling supplements containing the new language.

USP General Chapters <659>, <661.1> <661.2> Packaging and Storage Requirements

The purpose of the revisions is to provide, through General Chapter <659>, a 3-year period for implementation of the requirements specified in General Chapters <661.1> and <661.2>, which otherwise would have become applicable on 1 May 2017; to reinstate requirements previously expressed in General Chapter <661> during this 3-year period; to enable early adoption of the requirements in General Chapters <661.1> and <661.2> at any time during the 3-year period *in lieu* of meeting the reinstated <661> requirements; and to remove the

exemption to General Chapter <661.1> for previously approved packaging systems.

Europe

European Medicines Agency (EMA)

EU and US MRA - regulators agree on mutual recognition of inspections of medicines manufacturers

Regulators in the EU and the US have agreed to recognise inspections of manufacturing sites for human medicines conducted in their respective territories on both sides of the Atlantic. The agreement will enable both the EU authorities and the US FDA to make better use of their inspection resources to help them to focus on other parts of the world where active pharmaceutical ingredients (APIs) and medicines for the EU or US markets are manufactured.

The agreement is underpinned by robust evidence on both sides of the Atlantic that the EU and the US have comparable regulatory and procedural frameworks for inspections of manufacturers of human medicines. Teams from the European Commission, EU national competent authorities, the EMA and the US FDA have been auditing and assessing the respective supervisory systems since May 2014, and have worked closely together to reach this agreement.

The agreement is an annex to the EU-US MRA which was signed in 1998 but is not yet implemented. Many provisions of the agreement have already entered into force and others will enter into force on 1 November 2017. By that date, the EU will have completed its assessment of the FDA and the FDA is expected to have completed its assessment of at least eight EU Member States, and will be gradually expanded to all Member States.

Readers should note that Article 9 of the MRA states in respect of batch testing "In the EU, as provided in Article 51 paragraph 2 of Directive 2001/83/EC and in

Article 55 paragraph 2 of Directive 2001/82/EC, the qualified person will be relieved of responsibility for carrying out the controls laid down in Article 51 paragraph 1 of Directive 2001/83/EC and in Article 55 paragraph 1 of Directive 2001/82/EC provided that these controls have been carried out in the United States, the product was manufactured in the United States and that each batch/lot is accompanied by a batch certificate (in alignment with the WHO certification scheme on the quality of medicinal products) issued by the manufacturer certifying that the product complies with requirements of the marketing authorisation and signed by the person responsible for releasing the batch/lot."

(In the past, I led the European Federation of Pharmaceutical Industries and Associations Working Party on these MRAs. It was so very frustrating to see the EU/USA MRA "kicked into touch" whilst the others progressed. I sincerely hope that the UK will be able to make arrangements post Brexit to continue with all the MRAs made whilst it was a member of the EU – MH.)

EMA and heads of national competent authorities discuss consequences of Brexit

The goal was to start discussing how the work related to the evaluation and monitoring of medicines will be shared between Member States in view of the United Kingdom's withdrawal from the EU.

Although negotiations on the terms of the UK's departure have not yet officially commenced and one cannot prejudge their outcome, work will now start on the basis of the scenario that foresees that the UK will no longer participate in the work of the EMA and the European medicines regulatory system as of 30 March 2019.

General principles for workload distribution will include:

- ensuring business continuity;
- maintaining the quality and



robustness of the scientific assessment;

- continuing to comply with legal timelines;
- ensuring knowledge retention, either by building on existing knowledge, or through knowledge transfer;
- assuring an easy implementation and medium- and long-term sustainability.

A follow-up meeting will take place on 5 July 2017.

Brexit – notice to marketing authorisation holders (MAHs) of centrally authorised medicinal products

Unless the withdrawal agreement establishes another date or the period is extended by the European Council in accordance with Article 50(3) of the Treaty on European Union, all Union primary and secondary law ceases to apply to the United Kingdom from 30 March 2019, 00:00h (CET). The United Kingdom will then become a 'third country'. In this regard, MAHs of centrally authorised medicinal products for human and veterinary use are reminded of certain legal repercussions, which need to be considered.

- EU law requires that MAHs are established in the EU (or European Economic Area (EEA)).
- Some activities must be performed in the EU (or EEA), related for example to pharmacovigilance, batch release, etc.

Preparing for the withdrawal is, therefore, not just a matter for European and national administrations, but also for private parties. MAHs may be required to adapt processes and to consider changes to the terms of the marketing authorisation in order to ensure its continuous validity and exploitation, once the United Kingdom has left the EU.

Questions and answers (Q&As) – UK withdrawal from EU-medicinal products within the framework of the Centralised Procedure

This first list of Q&As has been drafted jointly by the European Commission and the EMA and concerns information related to establishment requirements within the EU (EEA). The Q&As will be further updated and complemented in the near future. There are currently nine Q&As covering the following.

- What if I am an MAH established in the UK?
- What if I am an orphan designation holder established in the UK? (for medicines for human use)
- What if I am a UK company with a MUMS (Minor Use Minor Species/limited market) status for my product? (for veterinary medicines)
- What if my qualified person for pharmacovigilance (QPPV) resides and carries out his/her tasks in the UK?
- What if my pharmacovigilance system master file (PSMF) is located in the UK? (for medicines for human use)
- What if my manufacturing site of the active substance is located in the UK?
- What if my manufacturing site of the finished product is located in the UK?
- What if my batch release site is located in the UK?
- I am a UK-based SME, would I still have access to financial and administrative assistance in accordance with Commission Regulation (EC) No 2049/2005 (the 'SME Regulation')?

(A similar set of requirements could well apply to license holders based in the EU for any product that they wish to export to the EU unless an MRA, some similar agreement, or a

transition arrangement is made. The Medicines and Healthcare Products Regulatory Agency (MHRA) could also insist upon (or be legally obliged to) inspecting EU-based companies as was the case before the UK joined the EU. It may also have to inspect UK API manufacturers to provide the necessary assurances to the EU regulators as required in Q&A 6 above. All despite the fact that EU and UK GMPs are aligned and likely to remain so through Pharmaceutical Inspection Cooperation Scheme (PIC/S) membership – MH.)

Report from the EMA-FDA quality-by-design (QbD) pilot program

The aim of this program was to facilitate the consistent implementation of QbD concepts introduced through International Council for Harmonisation (ICH) Q8, Q9 and Q10 documents and harmonise regulatory decisions to the greatest extent possible across the two regions.

Overall, it is concluded that, on the basis of the applications submitted for the pilot, there is solid alignment between both Agencies regarding the implementation of multiple ICH Q8, Q9 and Q10 concepts. The FDA/EMA QbD pilot program opened up a platform for continuous dialogue which may lead to further communication on areas of mutual interest to continue the Agencies' support for innovation and global development of medicines of high quality for the benefit of patients.

Both agencies are currently exploring potential joint activities with specific focus on continuous manufacturing, additional emerging technologies, and expedited/accelerated assessments (e.g. PRIME, Breakthrough). Additionally, the EMA and FDA are hosting experts from each other's organisations to facilitate dialogue and explore further opportunities.



Question and Answers on Implementation of Risk Based Prevention of Cross Contamination in Production and 'Guideline on Setting Health Based Exposure Limits for Use in Risk Identification in the Manufacture of Different Medicinal Products in Shared Facilities'

There are 14 Q&As in this document covering several topics.

- Must health based exposure limits (HBELs) be developed for all products? (Q1)
- What products/active substances are considered to be highly hazardous? (Q2)
- Could occupational exposure limits (OELs) or occupational exposure bands (OEBs) be used to support assessment of products to determine whether they may be highly hazardous? (Q3)
- Can calculation of HBELs be based on clinical data only (e.g. to establish the HBEL on 1/1000th of the minimum therapeutic dose)? (Q4)
- How can limits for cleaning purposes be established? (Q6)
- Where products for paediatric populations are manufactured in shared facilities with products intended for administration to adults or to animals, do the HBELs need adjustment? (Q11)

Deadline for comments was 30 April 2017. The MHRA has also published a guideline linked to the EMA document.

Reporting irregularities that may affect medicines

The EMA Board has adopted a new policy on handling information on alleged improprieties from external sources. These improprieties may include allegations of departures from standards of good practices that could have an impact on the evaluation and supervision of medicines.

The goal is to create an environment where individuals from

outside the Agency feel confident to raise their concerns on improprieties in their area of work. The policy helps the EMA assess these reports and coordinate any further investigation in a structured way, while protecting the confidentiality of the reporter.

New EudraVigilance system for collection and monitoring of suspected adverse reactions

The EMA will launch a new and improved version of EudraVigilance, the European information system of suspected adverse reactions to medicines that are authorised or being studied in clinical trials in the EEA. The new version of EudraVigilance will go live on 22 November 2017 with enhanced functionalities for reporting and analysing suspected adverse reactions.

Users of the system, i.e. national competent authorities, MAHs and sponsors of clinical trials, have to make final preparations to ensure that their processes and local information technology infrastructure are compatible with the new system and the internationally agreed format.

This EMA Management Board endorsement starts the countdown for stakeholders to get ready for the launch of the improved system in November 2017.

European Directorate for the Quality of Medicines (EDQM) Concept Paper on the Need for Revision of Note for Guidance on Quality of Water for Pharmaceutical Use

The current guideline needs to be updated to reflect imminent changes in the European Pharmacopoeia (Eur. Ph.). The text of the guideline needs to be updated to take into account manufacturing practices using methods other than distillation for producing water of injectable quality and the consequent deletion of the monograph "Water, highly purified". A new Eur. Ph. monograph "Water for preparation of extracts" (2249) is also published.

The objective of the guideline is to provide guidance to the industry on the pharmaceutical use of different grades of water in the manufacture of APIs and medicinal products for human and veterinary use. The intention of the revision is to be in line with the revised Eur. Ph. monograph for "Water for injections" (0169) and the consequent future deletion of the monograph "Water, highly purified" (1927). Comments were due by 6 June 2017.

Test for abnormal toxicity: towards possible deletion from the Eur. Ph.

The Eur. Ph. Commission is seeking public feedback on its proposal to remove the requirements for a test for abnormal toxicity from 49 monographs of the Eur. Ph. This consultation will run until June 2017 for all users, and will be extended until August for National Pharmacopoeia Authorities.

Top Ten Deficiencies - New Applications for Certificates of Suitability for Chemical Purity

This document is a summary of the 10 most FAQs raised after the initial evaluation of new applications for certificates of suitability (CEPs) for chemical purity. The top 10 FAQs are listed together with expectations and recommendations on how to address the specific deficiencies, with reference to applicable guidelines.

This document is intended to help applicants to improve the quality of their dossiers, in order to facilitate and speed up the granting of their CEPs. It should be taken into account while building up a dossier, in combination with the EDQM guideline "Content of the Dossier for Chemical Purity and Microbiological Quality (PA/PH/CEP 04 1)" available on the EDQM website. The top 10 deficiencies are as follows.

- Absence or deficient discussion on the risk of having potential mutagenic impurities in the final substance.



- Absence or insufficient discussion on fate and carryover of related substances of starting materials to the final substance.
- Lack of details and/or poor description of the manufacturing process of the substance from the introduction of starting materials
- Non-acceptable starting materials, necessity to redefine them earlier in the process.
- Non-adequate or poorly justified specifications in place to control the quality of starting materials.
- Non-adequate or missing specifications (and analytical methods) for reagents and solvents (recovered and recycled included) used to manufacture the substance from the introduction of starting materials.
- Non-adequate or missing discussion on carryover of reagents and elemental impurities to the final substance.
- Non-adequate or poorly justified specifications in place to control the quality of isolated intermediate.
- Absence or insufficient discussion on fate and carryover of impurities from synthetic intermediates (included) to the final substance.
- Non-adequate or missing information on the synthesis of starting materials and their manufacturers.

Biosimilars: Eur. Ph. monographs are flexible and evolving standards

During a seminar co-organised with the EMA, the EDQM clarified further the role that the Eur. Ph. monographs play in the assessment of biosimilars. As public standards for the quality of medicines in Europe, monographs ensure the quality of biosimilar and other biotherapeutic products, but compliance with them is not sufficient for demonstrating

biosimilarity. However, while Eur. Ph. monographs provide specifications in the form of tests and acceptance criteria for all medicines, they are dynamic documents that can be adapted to scientific progress.

Dr Peter Richardson, Head of Quality at the EMA, provided information on EU legislation in the field of biosimilars, and Dr Niklas Ekman, Senior Researcher at the Finnish Medicines Agency shared his experience as an assessor.

Management of Applications for New Certificates of Suitability and Requests for Revisions or Renewal of Certificates of Suitability
PA/PH/CEP (13) 110, which described the policy for assessment of CEP applications, has been revised following a review of current practice. As a result of the review, a three-round policy has been adopted for the assessment of applications and this is reflected in the revised document.

This policy change reflects the changing circumstances since the previous policy was adopted, in particular the increasing requirements for applicants to redefine starting materials to an earlier point in the synthetic route.

A similar policy is now applied to the assessment of requests for revisions/renewals of certificates and, therefore, this is incorporated in the revised document. The document PA/PH/Exp. CEP /T (04) 18, "Procedures for management of revisions/renewals of certificates of suitability to the European Pharmacopoeia monographs" has, therefore, been withdrawn.

Co-ordination group for Mutual recognition and decentralised procedures - human (CMDh) Q&A - qualified person (QP) declaration

The CMDh of the Heads of Medicines Agencies (HMA) has revised its Q&A document on the QP declaration. The update covers the types of QP declarations that must be submitted to support individual changes to marketing

authorisations covering the QP declaration(s) required to support individual types of changes to a marketing authorisation, to confirm that the active substance is manufactured in accordance with the detailed guidelines on GMP for starting materials?

Answers are given to cover the different scenarios: API manufacturer, finished product manufacturer and batch release site.

MHRA

MHRA GMP Inspection Deficiency Data Trend 2016

The GMDP (good manufacturing and distribution practice) Inspectorate has improved the way of gathering the inspection deficiency data for 2016. The new data trending can allow industries to identify the following.

- The severities and frequencies by the EU GMP references.
- The overall number of deficiencies by categories: Critical, Major, Other.
- The high impact versus high frequency issues.

The purpose for publishing the inspection deficiency data is to allow industries to perform their own assessment against the deficiency findings as part of self-inspection and continuous improvement.

MHRA GDP Symposium 2016

The MHRA has published a summary of this event on its blog. An exploration of company culture highlighting the way individuals interact, use processes and the effect that this has on compliance was the main theme. Topics covered included the Falsified Medicines Directive; whistleblowing and enforcement; error chains; and the Defective Medicines Reporting Centre.

Computer System Validation - GCP

This blog post is a combination of a case study seen at a single organisation and some of the



common findings good clinical practice (GCP) inspectors have seen across a number of recent inspections.

Import of centrally authorised medicines for supply to other Member States where the medicine is not yet available in the correct pack

The MHRA notes in this short blog that occasionally it receives notifications for import of centrally authorised medicines for supply to other Member States where the medicine is not yet available in the correct pack for their market and where the Member State may regard the supply to be intended to meet special needs of individual patients in the absence of an available licensed medicine.

The MHRA will object to notifications for import of an unlicensed medicine submitted in this manner on the grounds that the medicine is in fact licensed and available. Consequently, it cannot be notified for import as an unlicensed medicine.

Too much pressure: a behavioural approach to data integrity (part 2)

Behavioural issues are often unsuitable for technical guidance, but the Inspectorate blog provides an opportunity to address this complex issue.

This second blog post of the series illustrates the issues from the first in the series through a scenario based on situations sometimes encountered during inspections, and the changes in organisational approach which can address some of the problems identified. Peter Baker, an investigator within FDA's China office based in Beijing, has addressed this issue during various recent industry workshops, including the 2016 International Data Integrity Workshop supported by regulators from the MHRA, the EDQM, the EMA, the China FDA, the US FDA, and the World Health Organization. This blog post summarises his presentation and provides additional insight into the concept

of "too much pressure" within a pharmaceutical testing laboratory.

(I would recommend the book "Why Employees Don't Do What They're Supposed to Do and What to do About it" [ISBN 0-07-134255-9] by Ferdinand F Fournies as excellent reading matter for management/trainers and operators on this topic – MH.)

International

PIC/S

Reaffirmed stance on proposed EU advanced therapy medicinal products (ATMP) GMP guidelines and gaps highlighted relating to patient safety

On 24 April 2017, PIC/S sent a letter in response to a reply received from the European Commission on 5 April 2017 in connection with PIC/S' stance on the proposed EU ATMP GMP guidelines, which it considers will not only lower GMP standards for ATMP at the risk of patients but also lead to an internationally non-harmonised approach to the implementation of GMP for ATMP. In its latest letter, PIC/S reaffirms its position and highlights gaps relating to patient safety, while welcoming the Commission's proposal for engagement with PIC/S on its initiative and seeking clarification on the scope of cooperation proposed.

Products

EMA recommends suspension of medicines due to unreliable studies from Micro Therapeutic Research Labs

The EMA has recommended suspending a number of nationally approved medicines for which bioequivalence studies were conducted by Micro Therapeutic Research Labs at two sites in India. The Agency also recommended that medicines not yet authorised but which are being evaluated on the basis of bioequivalence studies from these sites should not be authorised until bioequivalence is demonstrated using alternative data.

The review of medicines studied by Micro Therapeutic Research Labs

was started after inspections to check compliance with GCP by Austrian and Dutch authorities in February 2016. The inspections identified several concerns at the company's sites regarding misrepresentation of study data and deficiencies in documentation and data handling.

The review, by EMA's Committee for Medicinal Products for Human Use (CHMP), concluded that data from studies conducted at the sites between June 2012 and June 2016 are unreliable and cannot be accepted as a basis for marketing authorisation in the EU.

EMA recommends changes to prescribing information for vancomycin antibiotics

The EMA has recommended changes to prescribing information for the antibiotic vancomycin to ensure appropriate use in the treatment of serious infections caused by Gram-positive bacteria, whilst ensuring appropriate use in the fight against antimicrobial resistance. Vancomycin remains an important therapeutic option for the treatment of serious infections. The Agency's CHMP reviewed the available data and made the following conclusions.

- Infusion of vancomycin can continue to be used for the treatment of serious infections caused by certain bacteria including methicillin-resistant *Staphylococcus aureus* in patients of all ages.
- Vancomycin can also be used to prevent bacterial endocarditis in patients undergoing surgery and to treat infections in patients undergoing peritoneal dialysis.
- The starting dose of vancomycin by infusion should be calculated according to the age and weight of the patient. The updated recommendations are based on data which showed that the previously recommended dose often resulted in less than optimal



levels of vancomycin in the blood, reducing the effectiveness of the antibiotic.

- When taken by mouth, use should be limited to the treatment of *Clostridium difficile* infections.

Because the available data do not adequately support the use of vancomycin in the treatment of staphylococcal enterocolitis and its use to clear the gut of bacteria in patients with a weakened immune (defence) system, the CHMP concluded that vancomycin should no longer be used for these indications. The CHMP opinion will be forwarded to the European Commission, which will issue a final decision valid throughout the EU in due course.

FDA approves first cancer treatment for any solid tumour with a specific genetic feature

The US FDA recently granted accelerated approval to a treatment for patients whose cancers have a specific genetic feature (biomarker). This is the first time the agency has approved a cancer treatment based on a common biomarker rather than the location in the body where the tumour originated.

Keytruda (pembrolizumab) is indicated for the treatment of adult and paediatric patients with unresectable or metastatic solid tumours that have been identified as having a biomarker referred to as microsatellite instability-high or mismatch repair deficient. This indication covers patients with solid tumours that have progressed following prior treatment and who have no satisfactory alternative treatment options, and patients with colorectal cancer that has progressed following treatment with certain chemotherapy drugs.

This is an important first; until now, the FDA has approved cancer treatments based on where in the body the cancer is – for example, lung or breast cancers. It now has approved a drug based on a tumour's biomarker without regard to the tumour's original location.

Extending expiration dates of doxycycline tablets and capsules in strategic stockpiles

A number of government public health and emergency response stakeholders maintain stockpiles of doxycycline tablets or capsules for post-exposure prophylaxis or treatment of inhalational anthrax in the event of an anthrax emergency. States have asked the FDA what would be necessary to provide confidence that stockpiled doxycycline tablets and capsules have retained their original quality (i.e. purity and potency) beyond the manufacturer's labelled expiration date so the replacement of stockpiled product could be deferred.

This document, once finalised, will provide guidance to government stakeholders on testing to extend the shelf life (i.e. expiration date) under section 564A(b) of the Federal Food, Drug and Cosmetic Act of stockpiled doxycycline tablets and capsules for public health emergency preparedness and response purposes for an anthrax emergency.

Conferences

EDQM Symposium on Microbiology planned for October 2017

The EDQM will hold an international symposium on 10–11 October 2017 in Strasbourg, France to present and discuss recent achievements, as well as future perspectives, of the Eur. Ph. in the microbiology field. The programme will cover, among others, topics such as rapid microbiology methods, including specific sessions on pharmaceutical water and cell therapy preparations; methods of preparation of sterile products; and biological indicators used in the manufacture of sterile products.

Documents

Association of British Pharmaceutical Industries (ABPI) manifesto

The manifesto 'Securing the Opportunity for UK Life Sciences by

2022' sets out the industry's three priorities to improve the use of medicines and grow the UK's status as a global hub for life sciences and pharmaceuticals. The ABPI calls on the next government to prioritise the following.

- Securing a world-class National Health Service (NHS) for patients – a strategy to make patient outcomes in the NHS the best in the world. This should start by increasing healthcare investment to the G7 average and ensuring the UK is in the top quartile of Organisation for Economic Co-operation and Development countries for patient access to new cost-effective medicines and vaccines by 2022.
- Securing global investment and jobs – a new industrial strategy that cements the UK's position as a leading global hub for the life science and pharmaceutical industry, attracting significant new international investment.
- Securing a new relationship with the EU that prioritises patient and public health – a new relationship with the EU that secures patient access to medicines and protects public health.

New Guide on Biosimilar Medicines for Healthcare Professionals – Increasing Understanding of Biosimilar Medicines

The objective of the guide published jointly by the EMA and the European Commission is to provide healthcare professionals with reference information on both the science and regulation underpinning the use of biosimilars. Biosimilars are biological medicines that are highly similar in all essential aspects to a biological medicine that has already been authorised.

EMA 2016 Annual Report

The report focuses on the Agency's key achievements in the areas of medicine evaluation, support to



research and development of new and innovative treatments and the safety monitoring of medicines in real life. In 2016, the Agency recommended a marketing authorisation for 81 medicines for human use, including 27 new active substances. On the veterinary side, 11 medicines were recommended for approval, including six new active substances. Approximately half of the applicants who were granted a positive opinion for their medicine had received scientific advice from the EMA during the development phase of their product.

The report also highlights some of the EMA's main projects, initiatives and achievements in 2016. These

include the launch of PRiority Medicines (PRIME), an initiative to support the development of medicines that address unmet medical needs and the policy on the publication of clinical trial data for new medicines, a ground-breaking new initiative that turned the EMA into one of the most transparent medicines regulators worldwide. Other developments include the EMA's contribution to addressing public health, including antimicrobial resistance and the Zika virus outbreak.

The report also contains three interviews on topics of major interest in the area of medicines and health in 2016.

- Vaccine hesitancy – a threat to public health.
- Creating an agile organisation for the 21st century.
- How to reinforce surveillance of antimicrobial consumption.

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@euromedcommunications.com

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PHARMA IN PLENARY

The rising costs of existing medicines in Europe

by Dr Nicola Davies

Rising costs of medicines in European healthcare systems is one of the major concerns for patients, advocates, governments, and other funding organisations that cover the cost of treatment. A review of the latest European Parliament questions, positions, and declarations relating to industrial pharmacy shows that increasing medicine costs are observed in specific therapeutic areas and within specific countries. This report provides a summary of the key issues relating to the rise in prices of certain medicines and the actions being taken to combat these issues.

The high cost of cancer treatments^{1,2}

Cancer is one of the therapeutic areas where treatment prices have skyrocketed in recent years. A specific aspect of this issue is that some drug makers increase the prices of cancer medicines that have long been in the market and have lost their market exclusivity. The price of generic medicines, ideally, should be close to the production cost.

However, a few drug manufacturers have increased the price of generic cancer treatments over the last 5 years, with some doing so by more than 1000%³. For example, Aspen Pharmacare Holdings Ltd. increased the price for the leukaemia generic drug, Busulfan, from 21 pence in 2011 to £2.61 in 2016. This is a 1143% price increase⁴. Another company, Actavis, has increased the cost of their hydrocortisone tablets by 9500% from £1.07 to £102.74³.

Aspen Pharmacare argued that the price increase was due to the fact that the generic drug, which has been in the market for the last 60 years, previously had a low-price base, which had stayed constant over the decades and has now become unsustainable⁵. However, patient advocates are concerned for cancer patients who may lose access to treatment due to "a desire for profit"³.

Price differences for existing medicines in the Netherlands⁶

The sudden increase in the prices for existing medicines is also an issue raised by pharmacists in the Netherlands. Specifically, new pharmaceutical organisations take over the production of medicines that have existed in the market for a long time and are still currently in use, attaching a higher price to these products. Dutch pharmacists refer to these drugs as "hijacked medicines"⁷.

Drug makers are not prohibited from increasing medicine prices, but the resulting scenario is that the medical insurance provider only reimburses the amount of the original price. Therefore, the burden of paying for the price difference falls on the patient. In a question posed to the European Commission regarding this matter, the Commission was asked to consider whether this pricing set-up constituted a fair and honest market⁷.

The high cost of medicines in Cyprus

Soaring prices can also be more common in specific European countries than in others. One such country is Cyprus, which is identified as historically having high-priced

medicines that results in poor access to treatment, especially for vulnerable segments of the population. Many drugs are also imported from other countries and so high prices may be partly due to unfavourable foreign exchange rates⁸.

Poor access to, and lack of affordability in, medicines is considered a breach in the fundamental European Union principle of equal and universal access to healthcare⁹. Therefore, the Commission is called upon to examine the unique pricing situation in Cyprus.

Actions being taken to combat rising costs

The European Commission is taking steps to address the various issues of drug pricing that may negatively impact patients' access to much-needed treatments.

An investigation into Aspen Pharmacare's alleged excessive pricing¹⁰

A formal investigation into price hiking concerns for five cancer medicines, including Busulfan, has been opened. The company at the centre of the investigation is Aspen Pharmacare, which acquired the companies that manufactured these five cancer drugs after the expiration of the products' respective patent protection periods. This is the first Commission investigation into a pharma company's alleged excessive pricing practice¹¹.

The Commission aims to find out whether the company imposed "very significant and unjustified price increases of up to several hundred percent", and whether the company used the price increase as leverage to threaten to withdraw the



medicines from certain markets⁷. Specifically, the investigation focuses on whether the company acted in breach of the EU Antitrust rules, which penalise the imposition of trading and pricing practices that create unfair conditions for customers¹¹.

An initiative for information exchange on health technology assessment and pricing policies²

Regarding the question posed on what the Commission is doing to help regulate the rising prices of cancer medicines, Commissioner Vytenis Andriukaitis has provided this response: "...the Commission is promoting improved exchange of information among Member States on their pricing policies to minimise negative effects on the accessibility of medicines and strengthening their cooperation on a voluntary basis; in particular through tools such as a European medicine price database (Euripid)"¹².

Andriukaitis added that the Commission recently conducted a public consultation, the aim of which was to drive an initiative to galvanise cooperation on health technology assessment across Member Nations and to share information and best practices for healthcare budget sustainability¹².

Promotion and support of price regulating measures²

The Commission also emphasises the need for Member States to implement measures, such as public procurement, promotion of generic and biosimilar use, and price-control policies, which promote and strengthen the accessibility, affordability, and cost-effective use of medicines. In addition, the

Commission has always shown support for authorities that facilitate national competition whenever they impose fines on pharma companies found to have conducted unfair trading practices and excessive pricing².

Appropriate and fair pricing is an essential method to not only ensure that patients have access to new treatments, but also continued access to existing medicines in the market. The Commission maintains that measures to regulate medicine prices and secure the delivery of care remain key priorities of Member States².

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bottled brown

Riding the Whirlwind

Curiosity

Our ability increases. Unexpected tragedies increase. They seem yoked together. Thalidomide (1956–1961) messed with unborn bodies and the minds and hearts of us all. Maybe tragedies are inevitable because “trial and error” is an essential part of the scientific method. The anthropologist Edmund Leach (1910–1989) observed that, “science offers us total mastery over our environment and over our destiny, yet instead of rejoicing we fell deeply afraid”. Imagine being feather duster worms. We would whisk our tentacles back into the safety of our cases. However, being human, we cannot help exploring.

The pharmaceutical industry entangles itself in risky situations. It boldly goes where nobody has gone before. An example is developing new drugs. The sociologist Daniel Bell (1919–2011) stated that we cannot know where innovations will go.

Risks

Consequences may be unintended. The kneejerk precaution of industry is some sort of insurance. Without it, much or all industry would halt. Some situations are highly novel. Then, risk is vastly greater. Another sociologist, Ulrich Beck (1944–2015), noted that innovative pharmaceutical companies face risks with three characteristics. Risks are of global reach. Once an accident has occurred, they cannot go back. They cannot push some “undo” command as on some computer

software. Adverse consequences have no limit on time and space.

One hazard hotspot with human volunteers is Phase I clinical trials. One with adverse consequences was TGN1412, an immunoregulatory drug first trialed in 2006. Another was BIA 10-2474, a human cannabinoid system interactor, in 2016.

Benefitting from the 20/20 vision of hindsight, we know now that the risks were greater than anticipated. Humans are poor at objectively assessing the magnitude of risks or balancing them. Some risks we feel intuitively are greater than they are. We seem to most fear those that happen quickly and can graphically imagine. One example is crashing our vehicle over a precipice. We construct guardrails there although their cost, if invested elsewhere, would increase safety more. Medicine package information leaflets list side effects. Likelihoods may use absolute frequencies to divide into very common, common, rare and very rare. However, if consequences include a serious disease or death, objective assessment is unlikely.

Solutions

How can the pharmaceutical industry protect against risk? It can use various sorts of human interaction. The anthropologist Alan Fiske (1947–) claims there are four types. One is to adjust price in a market. This needs money, technologies and mathematics. The capitalist pharmaceutical industry must change sufficiently during drug patent periods. That recoups, at least, the costs of adverse

consequences. As businesses, they must continue to make a profit.

That demands rare and learned expertise. Good luck, if not a god-like foresight, also help.

Another method is matching exchanged gifts or bartering, tit-for-tat. Industry pays its human clinical trial volunteers. They presumably ponder risks before choosing involvement. However, volunteers are vulnerable. They deserve to be fully informed. However, even the most able experts are uncertain about the effect in healthy humans at that time — hence the trial. Society judges harshly any company inflicting harm.

A third method is that the powerful confiscate. The pharmaceutical industry seethes with takeovers; the strong swallow the weak including the less powerful company's intellectual property, such as clinical trial data. The fourth method merits consideration in today's uncertain world of greater risks. Share profits and risks without counting the cost. One strategy is cooperation with the state or states somewhere on a spectrum. That includes following guidance from the European Medicines Agency, collaboration with academia and nationalisation. The latter seems unlikely. But so, we were told, were Brexit or President Trump.

Malcolm E Brown



General Assembly held in Malta 20-21 May

During the General Assembly, Anni Svala (Suomen Farmasialiitto, Finland) was re-elected as Vice-President Education and Training and Giorgos Panoutsopoulos (Panhellenic Association of Pharmacists, Greece) was elected as Vice-President Communications for the next 3 years.

The EIPG Past Presidents Award was conferred on Jean Pierre Paccioni, who was also declared an EIPG Fellow, while Valerie Lacamoire was given the EIPG Outstanding Service Award. The awards were collected on behalf of both awardees by EIPG Treasurer and French delegate Brigitte Saunier. On behalf of the Association in Ireland, Pharmacists in Industry, Education and Regulatory, Helen Naddy collected the EIPG President's Award for excellent support on webinars, while on behalf of the Italian Association, Associazione Farmaceutici dell'Industria (AFI), EIPG Vice-President and Italian delegate Piero Iamartino also collected the EIPG President's Award for outstanding support and commitment to EIPG shown by AFI throughout the year. Michael Bittermann accepted an award for sponsorship on behalf of Aesica Pharmaceuticals, Tricia Kennerly on behalf of Walgreens Boots Alliance and Joanna Gatt on behalf of Vivian Corporation.

Working Group on Quality Systems in Serialisation

The focus of this Working Group was on the implementation of quality systems in serialisation, both in manufacture and throughout the supply chain.

The licence holder is responsible for the release of the product into the market and, therefore, the marketing authorisation holder (MAH) must rely on the manufacturing site to perform a robust final step in the packaging process to produce a reliable barcode system. The MAH must

ensure that the packaging material is properly designed and approved by the Competent Authority in order to allocate the correct and readable barcode to guarantee its traceability and reconciliation. The barcode generation and management systems should be able to interface with the systems adopted by any on-boarding partners. The barcode must be transferred in an approved artwork that is sent to the packaging supplier. The barcode can be pre-printed on each carton or adequate space must be left for on-line printing. The packaging site must ensure that the supplier is fully qualified to perform this work and be in possession of the necessary equipment and procedures to avoid any mix-up or mistake during each step in the process flow.

At the packaging site, it is the responsibility of the manufacturer to qualify and periodically assess the packaging equipment's performance in terms of reliability and repeatability to ensure that it is able to print, read and upload the barcode, in the repository system, of each package available for the supply chain. This last step is critical because it is important to ensure that all the information in the barcode is completely transferred to the repository system (data integrity aspects and big data management).

During the packaging steps, the quality system should ensure that rejected, damaged and retained samples are not part of the commissioning of the product and a final reconciliation must be performed to ensure that these aspects were properly managed. If the MAH assigns the packaging activity to a third party contract manufacturer, it is their duty to qualify and approve this supplier. A technical agreement needs to be in place indicating the responsibility of each aspect impacting on the quality, safety and efficacy of the product, including anti-counterfeit measures, such as the unique identifier.

Repackaging or relabelling of a product already commissioned in

the repository system requires strict control of the change in barcode because all the involved packs have to be decommissioned and commissioned again to trace the change of code. In this case the reconciliation at the end of the process is strictly required.

Points of reflection include the recently revised Annex 16 of the EU Guidelines to Good Manufacturing Practice, which contains few indications for addressing qualified persons responsibilities in relation to the Delegated Act and the impact on Annex 21, the new guidance for importers of medicinal products. Also, the role and interaction with countries that have Mutual Recognition Agreements with the EU will need to be considered.

Working Group on Value-based Outcomes in the Pharmaceutical Industry

As life expectancy in Europe is rapidly increasing, what is certain is that more and more people will be living with a chronic disease, become susceptible to cancer and/or life-style/age-related conditions. The impact on society, the strain on healthcare systems and the drive to provide innovative medicines to improve standard of care cannot be underestimated and is leading to an unsustainable healthcare model. Hence, expectations on the industry to work with government/regulatory bodies to demonstrate value-based outcomes is expected to rise and rise. Recommendations for EIPG from this working group are as follows.

1. Increase/encourage interaction between healthcare practitioners and industrial pharmacists.
2. Maximise continuing professional development opportunities.
3. Prepare a position paper on connected data/precision medicine for submission to the Commission.

4. Work with the European Association of Hospital Pharmacists and the Pharmaceutical Group of the European Union to put the pharmacist at the forefront of patient care whether it be in the patients' home or at the surgery.
5. As waste is a key issue, it should be discussed between pharmacists working in community, hospital and industry and the Commission.
6. The pan-European infrastructure (as for pharmacovigilance) should be harnessed to support evidence-based practice.

Symposium

A scientific symposium entitled "Precision Medicine: Paradigm Shifts for Millennial Patients" was held on the Friday before the General Assembly. Dr Patricia Bonanno, a member of the Management Board of the European Centre for Disease Prevention and Control and a member of the Horizon 2020 Advisory Group on Nanotechnology, Advanced Materials, Biotechnology and Advanced Manufacturing Processing was the moderator. The opening speaker was the Hon Dr Miriam Dalli, MEP, who addressed the audience via a recorded video message on the importance of specialist health matters, such as precision medicine.

Mr Martin Seychell, Deputy Director-General for Health, DG SANTE, discussed access to innovative medicines in the EU. He mentioned that the Commission held conferences in 2011 and 2016 and that there had been a meeting on the applicable technologies in 2013. Three billion euros have already been spent on health research and some of this is to align and encourage capacity in personalised medicine. A policy paper about the management of rare diseases has been completed by 126 academics and industrial

personnel. A number of proposals have been put forward for improved diagnosis and treatment of rare diseases involving 26 countries. State of the art technology is involved and expected to support better patient outcomes. There is a need for mobile health services and a renewed focus on access to personalised health, including a secure infrastructure and interaction between digital health treatments to provide equitable access to medicines. He felt it was important to build on sustainable action, to update achievements, avoid duplication, and to map forward to 2020 where priorities will be set on how and where we want to invest.

Dr Barbara Freischem, Executive Director, European Biopharmaceutical Enterprises (EBE) within the European Federation of Pharmaceutical Industries and Associations (EFPIA) was the next speaker. She noted that we are moving away from all patients being "all the same" and we need to understand the disease biology in order to provide diagnoses. This provides regulatory challenges for a diagnostic product marketed together with a medicinal product. There is limited patient access to personalised medicine in Europe and there is a need for a European framework supportive of emerging innovation.

The key regulatory challenges are that Notified Bodies undertake checks on diagnostics and what happens if they disagree with the European Medicines Agency (EMA) which has to register the medicinal product? How will labelling decisions be coordinated between the medicinal product and its companion diagnostic? A concept paper has been issued by the EMA and a workshop is planned. A framework document explains how one can tease out patients for whom the treatment will be beneficial. The evolution of tests with multiple markers will lead to a patient treatment pathway. Both the EFPIA and EBE are working on each of the challenges that hamper

personalised medicines from becoming a reality.

Tricia Kennerly, Vice-President, Walgreens Boots Alliance, discussed the delivery to patients of precision medicines. Alliance Healthcare has 390 distribution centres in 20 countries and precision medicines are expensive compared to conventional medicines. Therefore, an increase in working capital is needed, new equipment and facilities must be provided, the stock holding ability will alter and loss or damage to the product will have to be taken into account.

Medicines innovation is driving non-traditional models with patient access schemes for unlicensed products and unforeseen future requirements involving clinical and regulatory aspects. Handling requirements differ with specific temperatures, fragile products, altered packaging, and handling of sterile products, and new facilities, new equipment, specialist training and revised standard operating procedures will all be necessary. She discussed the Alcura cold chain validation needed for efficient and responsive distribution of biomarkers and their drug treatments. Patient support increases with a need for support programmes, pharmacy versus home care delivery, adverse event profiles, new training, funding, batch recall, labelling, tracking and tagging. Pharmacists will need training as there will be more outcome measurements, creating entirely new big data sets.

The last speaker was Dr Romina Britta, a post-doctoral research fellow from the University of Malta currently on a scholarship with the University of St Andrews, Scotland. She is a specialist in molecular pathology, specifically in the field of colorectal cancer. Her area of interest is in basic and translational research (data mining, patient cohorts and biobanks) towards development of predictive and theranostic biomarkers. She explained precision medicine from one size fits all towards medical

models that use molecular profiling. This can be from developing drugs on the basis of “one gene, one drug” to “multi-gene, multi-drug” models that establish which drug fits which patient at the highest efficiency.

Biomarkers are diagnostic products that can predict individuals at higher risk of developing a disease. Prognostic biomarkers indicate the likely progression of the disease. In addition, there are predictive and surveillance biomarkers. Basic research has shown the development of disease and translational research has moved from the bench to the bedside. Pre-clinical test mouse models are cell-line derived xenograft *in vivo* models. Organoids as models may fill the gap between cancer genetics and patient trials. She described one of the technologies “Clustered regularly interspaced short palindromic

repeats” (CRISPR) as a powerful functional tool and “Complimentary functional analysis”, such as image cytometry for plate-based assays, as very expensive.

There is obvious improved clinical impact with patient stratification, and biomarkers can inform clinical decisions. A new regulatory environment will be needed as “systems medicine” is a way of thinking. There needs to be more collaboration and equal partnerships between academia, industry and clinicians.

In response to a question from Gino Martini on “big data”, Martin Seychell agreed that we do not really exploit data and that it was little used to optimise patient treatment. The Commission are working on a plan for digital health and the need to standardise data. The problem has been that Governments have not been able to put data “on the table”, and there

needs to be greater trust between healthcare systems and industry on data ownership.

In response to a comment from Amon Wafelman on government manufacturing sites, it was felt that the Commission should work together with Member States, define and adapt the tools and be flexible. New technologies are forcing us to face reality.

In his closing remarks, Claude Farrugia said that as “big data” important to patient care becomes available along the supply chain, we should be considering accessibility and “make haste with responsibility”.

The slides shown by Dr Frieschem and Ms Kennerley during the above Symposium presentations are available on the EIPG website.

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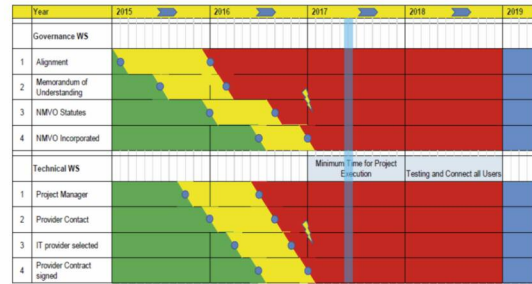


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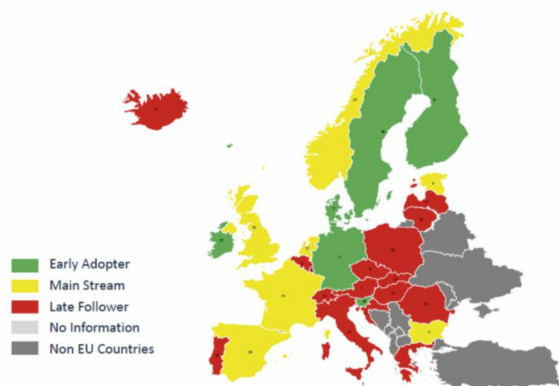
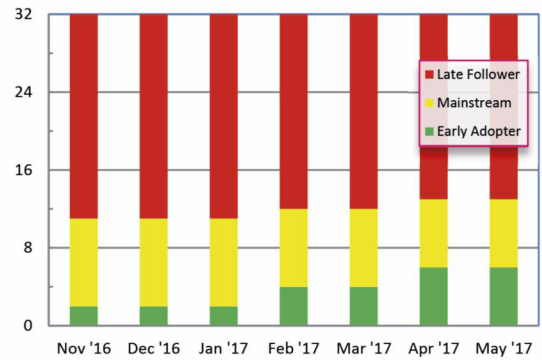
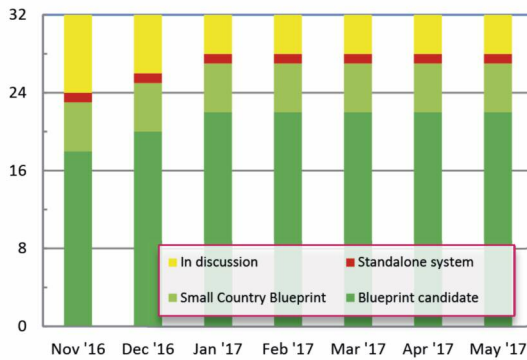


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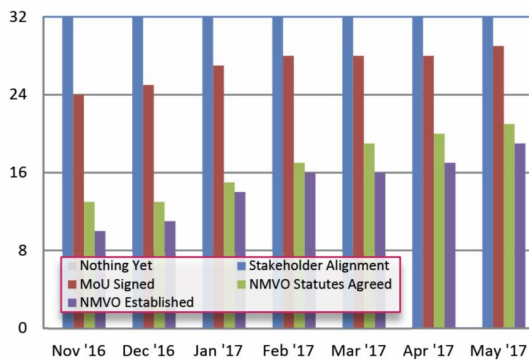
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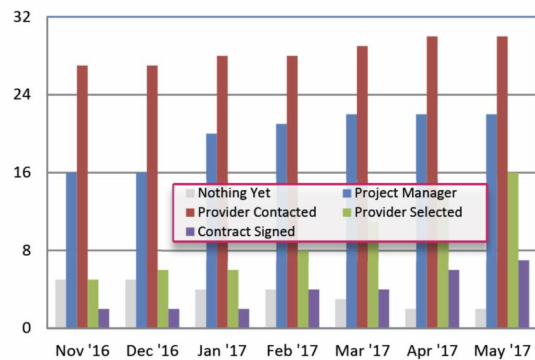
Blueprint Tendency



Governance Workstream



Technical Workstream



events

JULY 2017

3–5 July 2017 – Bangkok, Thailand
4th Annual Congress on Drug Discovery & Designing
<http://drugdiscovery.pharmaceuticalconferences.com>

10–11 July 2017 – Jakarta, Indonesia
8th Global Pharmacovigilance & Drug Safety Summit
<http://globalpharmacovigilance.pharmaceuticalconferences.com/>

10–12 July 2017 – Madrid, Spain
9th Annual European Pharma Congress
<http://europe.pharmaceuticalconferences.com/>

17–19 July 2017 – Munich, Germany
9th International Conference and Exhibition on Pharmacovigilance & Drug Safety
<http://pharmacovigilance.pharmaceuticalconferences.com/>

24–25 July 2017 – Rome, Italy
13th International Conference and Exhibition on Nanomedicine and Pharmaceutical Nanotechnology
<http://nanotechnology.pharmaceuticalconferences.com/>

31 July–1 August 2017 – Milan, Italy
3rd World Congress and Exhibition on Antibiotics and Antibiotic Resistance
<http://antibiotics.pharmaceuticalconferences.com/>

AUGUST 2017

17–18 August 2017 – Los Angeles, CA, USA
8th Annual Global Pharma Summit
<http://www.clocate.com/conference/8th-Annual-Global-Pharma-Summit-2017/62641/>

31 August–1 September 2017 – Las Vegas, NV, USA
5th International Pharmacy Conference
<http://pharmacy.pharmaceuticalconferences.com/>

SEPTEMBER 2017

5–7 September 2017 – Hatfield, UK
8th International PharmSci Conference 2017
www.apsgb.co.uk

7–9 September 2017 – Paris, France
6th World Congress on Biopolymers
<http://biopolymers.conferenceseries.com/>

10–14 September 2017 – Seoul, Republic of Korea
77th FIP World Congress of Pharmacy and Pharmaceutical Sciences 2017
<http://www.fip.org/seoul2017/>

11–13 September 2017 – Washington, DC, USA
PDA/FDA Joint Regulatory Conference
www.pda.org

20–21 September 2017 – Dublin, Ireland
3rd International Conference on Advanced Clinical Research and Clinical Trials
<http://clinicalresearch.pharmaceuticalconferences.com/>

25–26 September 2017 – Chicago, IL, USA
6th International Conference and Exhibition on GMP, GCP & Quality Control
<http://gmp-gcp-quality-control.pharmaceuticalconferences.com/>

25–26 September 2017 – Chicago, IL, USA
7th International Conference and Exhibition on Pharmaceutical Regulatory Affairs and IPR
<http://regulatoryaffairs.pharmaceuticalconferences.com/>

25–27 September 2017 – Vienna, Austria
3rd International Conference and Expo on Drug Discovery & Designing
<http://drugdiscovery.pharmaceuticalconferences.com>

26–27 September 2017 – Dublin, Ireland
2017 Europe Biotechnology Conference
www.ispe.org

OCTOBER 2017

9–10 October 2017 – San Diego, CA, USA
4th Annual Drug Discovery USA Congress
<http://www.discoveryusa-congress.com/>

10–11 October 2017 – Strasbourg, France
EDQM Symposium on Microbiology
<https://www.edqm.eu/en/news/edqm-symposium-microbiology-planned-october-2017>

10–11 October 2017 – Prague, Czech Republic
Pharmaceutical Cold & Supply Chain Logistics
www.pda.org

10–12 October 2017 – Barcelona, Spain
World Vaccines Conference Europe
<http://www.terrapinn.com/conference/world-vaccine-congress-europe/index.stm>

16–17 October 2017 – San Francisco, CA, USA
10th International Conference and Exhibition on Biologics and Biosimilars
<http://biosimilars-biologics.pharmaceuticalconferences.com/>

16–18 October 2017 – Baltimore, MD, USA
11th World Drug Delivery Summit
<http://drugdelivery.pharmaceuticalconferences.com/>

16–18 October 2017 – Budapest, Hungary
12th World Pharma Congress
<http://world.pharmaceuticalconferences.com/>

19–20 October 2017 – Seoul, Republic of Korea
9th Annual Congress on Drug Design & Drug Formulation
<http://drugformulation-bioavailability.pharmaceuticalconferences.com/>

