PHARMACEUTICAL PHYSICIAN

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Healthcare technology

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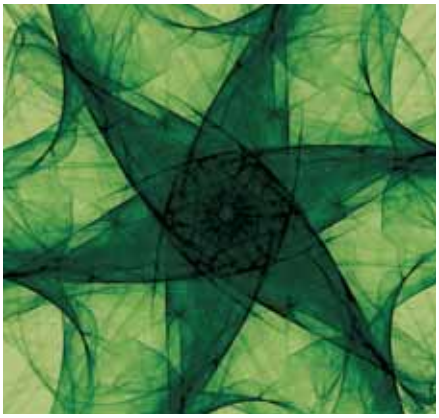

MARCH 2017 **VOLUME 27 | Nº2**

JOURNAL OF THE BRITISH ASSOCIATION OF PHARMACEUTICAL PHYSICIANS

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IN AN ISSUE that spans blue frogs, translational medicine and innovations in technology, there must be something for everyone here.

Anne Hetherington has provided a tour de force Regulatory Roundup: our colleagues at the agencies have been very busy over the past months and I spotted several new guidelines that I need to get to grips with. Thank you, Anne.

In a thoughtful and thought-provoking article, Matt Goodman considers the real impact that health technologies are already having on patients and the collection of their precious data- and what still be to come. There are some shining examples of the positive contribution that appropriately deployed technology is already making in some areas of the UK for example, Airedale where telemedicine is a reality. We've come a long way already but there is still a lot of potential.

The "Wellcome Trust exists to improve health for everyone by helping great ideas to thrive. We have a proud history of backing great scientists to develop their ideas from fundamental research to an impact on human health," notes Professor Steve Caddick as he describes the WT's new way of working in a modern world. So many programmes progressing well today would not have even started without the vision and appetite for innovation which underpins a WT grant and this new approach is very exciting.

Biosimilars have been very topical. We have moved from 'it's too hard, no one will ever really manage it' to approved products. Matt Hickling wrote on the topic back in 2010 and his article bears re-reading today.

"The world is run by those who show up"- read on as Katie L Chain MS shares more pearls of wisdom for the ambitious amongst you (or even those who just want to get home on time...)

News from the MHRA on the new MedRegs blog and an introduction to two new health economists who have joined the Office for Health Economics. Health economics and outcomes research certainly does seem to be a booming discipline and more important to each of us by the day.

Big plug: Buy Faiz Kermani's storybook for children: the money is going to the World Medical Fund to support paediatric clinics in Malawi and it makes a pleasant change to read about a blue frog instead of a green caterpillar!

Dr Madhu Davies

Dr Madhu Davies

REGULATORY ROUND UP

By Anne Hetherington, Senior Regulatory Consultant, Envigo Ltd.

HERE IS THE LATEST ROUND UP OF REGULATORY NEWS FROM THE LEADING AGENCIES, INCLUDING THE EUROPEAN MEDICINES AGENCY (EMA), THE MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA) AND THE FOOD AND DRUGS ADMINISTRATION (FDA). EMPHASIS IS PLACED ON THOSE NEW REGULATIONS WHICH IMPACT ON CLINICAL AREAS.

PLEASE CLICK ON THE LINKS BELOW TO TAKE YOU TO THE RELEVANT ITEM.

WE HOPE THAT YOU WILL FIND THIS DIGEST OF INTEREST. IF YOU HAVE ANY COMMENTS OR QUERIES PLEASE CONTACT US AT INFO@ENVIGO.CO.UK.

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Anne Hetherington

1. EUROPEAN MEDICINES AGENCY (EMA)

News and press releases

- Proposals to revise guidance on first-in-human clinical trials
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/07/news_detail_002572.jsp&mid=WC0b01ac058004d5c1

- Statement on the outcome of the UK referendum
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/07/news_detail_002566.jsp&mid=WC0b01ac058004d5c1

- Data integrity: key to public health protection
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/08/news_detail_002589.jsp&mid=WC0b01ac058004d5c1

- Transparency in drug regulation
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/08/news_detail_002587.jsp&mid=WC0b01ac058004d5c1

- Implementation of the pharmacovigilance legislation (updated)
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000520.jsp&mid=WC0b01ac05804fa031

- Addressing challenges of innovative cancer immunotherapy medicines
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/08/news_detail_002591.jsp&mid=WC0b01ac058004d5c1

- Final report on the adaptive pathways pilot
  http://www.ema.europa.eu/docs/en_GB/document_library/Report/2016/08/WC500211526.pdf

- Transparency in drug regulation
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/08/news_detail_002587.jsp&mid=WC0b01ac058004d5c1

- Implementation of the pharmacovigilance legislation (updated)
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000520.jsp&mid=WC0b01ac05804fa031

- Addressing challenges of innovative cancer immunotherapy medicines
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/08/news_detail_002591.jsp&mid=WC0b01ac058004d5c1

- Treatment and prophylaxis of respiratory syncytial virus (RSV) infection
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001752.jsp&mid=

- How to make better use of patient registries to collect high-quality data on medicines
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/10/news_detail_002627.jsp&mid=WC0b01ac058004d5c1

- Influenza vaccines - non-clinical and clinical module
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001360.jsp&mid=WC0b01ac058002958b

- Development challenges for medicines for central nervous system disorders
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/11/news_detail_002654.jsp&mid=WC0b01ac058004d5c1

Updates

- Concept paper on the revision of the 'Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products'
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500210825.pdf

- Clinical Trial Regulation (updated)
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000629.jsp&mid=WC0b01ac05808768df

- Guideline on the clinical development of medicinal products for the treatment of HIV infection, adopted
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500209918.pdf

- Guideline on clinical evaluation of medicinal products used in weight management, adopted
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500209942.pdf

- Clinical investigation on medicinal products in the treatment of hypertension (updated)
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001069.jsp&mid=WC0b01ac0580034cef

- Clinical investigation of medicinal products in the treatment of lipid disorders (updated)
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001073.jsp&mid=WC0b01ac0580034cef

- Draft guideline on the clinical evaluation of direct acting antivirals for the treatment of chronic hepatitis
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500209917.pdf

- Guidance for companies considering the adaptive pathways approach (updated)
  http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2015/11/WC500196726.pdf

- Questions and answers on signal management (updated)
  http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/09/WC500150743.pdf

- EudraVigilance - Inclusion/exclusion criteria for the "Important Medical Events" list
  http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/08/WC500212100.pdf

- Guideline on potency testing of cell based immunotherapy medicinal products for the treatment of cancer - Revision 1, adopted
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211641.pdf

- Draft guideline on the development of new medicinal products for the treatment of Crohn's Disease - Revision 2: consultation open
  http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500211430.pdf

- Draft guideline on the development of new medicinal products for the treatment of Ulcerative Colitis - Revision 1: consultation open
  *http://www.ema.europa.eu/docs/en_*

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GB/document_library/Scientific_guideline/2016/07/WC500211431.pdf

- Draft addendum to the 'guideline on the evaluation of medicinal products indicated for treatment of bacterial infections' to address the clinical development of new agents to treat disease due to Mycobacterium tuberculosis - Revision 1: consultation open *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211447.pdf*

- Concept paper on the need for revision of the guideline on the clinical development of medicinal products for the treatment of cystic fibrosis (CHMP/EWP/9147/2008) - Revision 1, draft: consultation open *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211478.pdf*

- Draft addendum to the 'guideline on the evaluation of medicinal products indicated for treatment of bacterial infections' to address the clinical development of new agents to treat disease due to Mycobacterium tuberculosis - Revision 1: consultation open *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211447.pdf*

- Concept paper on the need for revision of the guideline on the clinical development of medicinal products for the treatment of cystic fibrosis (CHMP/EWP/9147/2008) - Revision 1 *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211478.pdf*

- Guidance for companies considering the adaptive pathways approach (updated) *http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2015/11/WC500196726.pdf*

- Questions and answers on signal management (updated) *http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/09/WC500150743.pdf*

- Guideline on potency testing of cell based immunotherapy medicinal products for the treatment of cancer - Revision 1, adopted *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211641.pdf*

- Guideline on development, production, characterisation and specification for monoclonal antibodies and related products - Revision 1, adopted *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211640.pdf*

- Draft addendum to the 'guideline on the evaluation of medicinal products indicated for treatment of bacterial infections' to address the clinical development of new agents to treat disease due to Mycobacterium tuberculosis - Revision 1: consultation open *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211447.pdf*

- Guideline on good pharmacovigilance practices (GVP): Product- or population-specific considerations II: Biological medicinal products, adopted *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/08/WC500211728.pdf*

- Guideline on the clinical investigation of medicinal products to prevent development/slow progression of chronic renal insufficiency, adopted *http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/10/WC500214980.pdf*

- ICH E11(R1) guideline on clinical

investigation of medicinal products in the pediatric population: Step 2b, draft: consultation open
http://www.ema.europa.eu/ema/doc_index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500214185&murl=menus/document_library/document_library.jsp&mid=0b01ac058009a3dc

- Strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products (updated)
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001001.jsp&mid=WC0b01ac0580029570

- Early access to medicines - Development support and regulatory tools (updated)
http://www.ema.europa.eu/docs/en_GB/document_library/Leaflet/2016/04/WC500204707.pdf

- How to facilitate development of cancer treatment based on genetically modified T-cells
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/11/news_detail_002638.jsp&mid=WC0b01ac058004d5c1

- Guideline on clinical investigation of medicinal products for prevention of venous thromboembolism (VTE) in non-surgical patients, adopted
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/11/WC500217355.pdf

- Draft guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products, draft: consultation open
http://www.ema.europa.eu/ema/doc_index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500216158&murl=menus/document_library/document_library.jsp&mid=0b01ac058009a3dc

EUROPEAN COMMISSION

- Study on the regulation of advanced therapies in selected jurisdictions
http://ec.europa.eu/health//sites/health/files/human-use/docs/20147306_rfs_chafea_2014_health_24_060516.pdf

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA)

- MHRA GxP Data Integrity Definitions and Guidance for Industry
https://www.gov.uk/government/news/mhra-gxp-data-integrity-definitions-and-guidance-for-industry

- MHRA and making a success of Brexit
https://www.gov.uk/government/news/medicines-and-healthcare-products-regulatory-agency-statement-on-the-outcome-of-the-eu-referendum

- Clinical Trials Regulations – have your say
https://www.gov.uk/government/news/clinical-trials-regulations-have-your-say

FOOD AND DRUG ADMINISTRATION (FDA)

Guidance for Industry

- Tracking genetic changes in West Nile Virus that could affect its spread and the ability of blood donor screening tests, future treatments, and vaccines to work effectively
https://www.fda.gov/BiologicsBloodVaccines/ScienceResearch/ucm512485.htm

- Ulcerative Colitis: Clinical Trial Endpoints Guidance for Industry
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM515143.pdf

- Revised Recommendations for Reducing the Risk of Zika Virus

Transmission by Blood and Blood Components; Guidance for Industry
https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/UCM518213.pdf

- Use of Nucleic Acid Tests to Reduce the Risk of Transmission of Hepatitis B Virus from Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Guidance for Industry
https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/UCM516650.pdf

- Low Sexual Interest, Desire, and/or Arousal in Women: Developing Drugs for Treatment Guidance for Industry
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidance/UCM526362.pdf

- Head Lice Infestation: Developing Drugs for Topical Treatment Guidance for Industry (PDF - 233KB)
https://www.fda.gov/downloads/Dru

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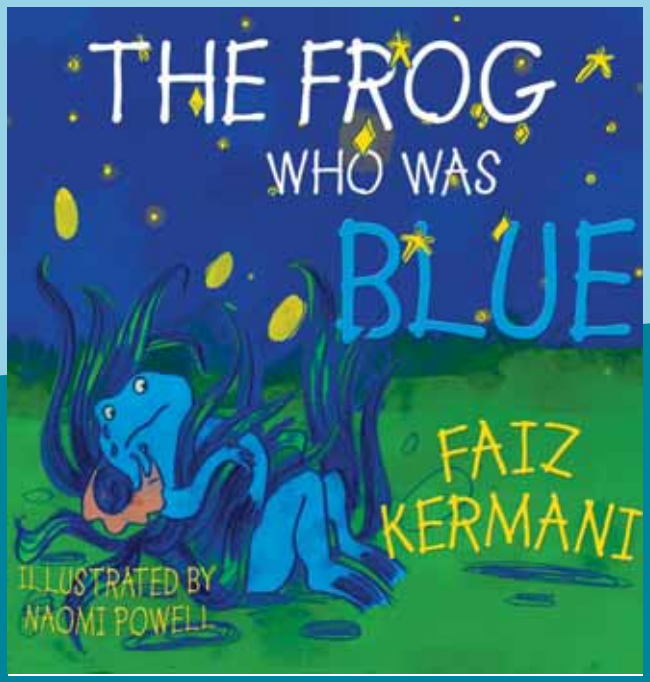
gs/GuidanceComplianceRegulatoryInformation/Guidance/UCM476999.pdf

- Reforming Clinical Trials in Drug Development: Impact of Targeted Therapies
  https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM530409.pdf

- Non-Inferiority Clinical Trials to Establish Effectiveness Guidance for Industry
  https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM202140.pdf

THE FROG WHO WAS BLUE



In Faiz Kermani's new children's novel, the loneliest frog in Malawi struggles to be accepted for his skin colour

Prolific children's author Faiz Kermani has returned with his new children's novel, The Frog Who Was Blue, which he's publishing for a good cause.

"In my free time I serve on the board of a children's medical charity called the World Medical Fund (WMF). WMF runs mobile health clinics in Malawi, treating more than 25,000 children every year.

"Since all children love to read, we thought that a children's book, with a story set in Malawi, might make for an entertaining diversion for those children attending the clinics," comments Faiz.

His new book features protagonist Biriwita, a blue frog who longs to be accepted at Croak College, the most famous school for frogs in Malawi.

However, they all turn their backs on him as he is just too different!

"What's wrong with you? Why are you blue? You're the strangest frog we've seen. Normal frogs are green!"

The Frog Who Was Blue is a witty and charming tale underpinned by the message that being different to others is no bad thing. "We hope that the book can raise the profile of WMF, since the charity's life-saving work relies entirely on donations," comments Faiz. "WMF's focus is on the region's poorest and most vulnerable children, including AIDS orphans."

More information about the WMF is on their webpage: www.worldmedicalfund.org.

Goodreads reviews of The Frog in the Skyscraper, Faiz's previous book:

"An adorable book... Great for young early readers"

"Such a cute story including nice illustrations... You'll enjoy it if you're a child or an adult!"

Away from his serious scientific day job, in his free time, FAIZ KERMANI loves writing children's books that have funny themes and has also published The Frog in the Skyscraper and The Frog Who Loved Mathematics. His books have won awards in the US and UK and have been translated into French, German, Spanish and Russian. He is also involved in various literacy projects with schools and non-profit work with healthcare charities.

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SPECIAL FEATURE:
Healthcare
In the Age of Technology

By Dr. Matthew Goodman MB.ChB, Dip.Pharm.Med., MFPM

Matthew Goodman

GETTING STARTED

DIGITAL HEALTH? EHEALTH? mHealth?, Telehealth?, Telemedicine?, Digital therapeutics? If you're confused by the lingo, you're not alone. Are these all the same thing? If not, what are the differences? And does it really matter if I'm a Pharmaceutical Physician? Let me explain, and in doing so maybe answer the important question – should I care?

Some nomenclature first, so that we are all on the same page. It's taking some time for the dust to settle on terminology, but increasingly the term 'Connected Health' is being used as a cover-all term to describe technology when applied to health. This may include such things as telecare, telehealth, telemedicine, mHealth, eHealth, and digital therapeutic services. If something involves software, primarily running on inter-connected devices to support or deliver healthcare, chances are you're looking at Connected Health. The key distinguishing features are that these are patient and clinician facing, and their intent is to improve health, not merely streamline processes in the background, for example clinical data sharing or appointment booking. Bear with me – we'll come back to this.

A BRIEF HISTORY

The first forays into Heath IT and therefore the forerunners of Connected Health hark back to the 1980's and early 90's. When the rise of computing power combined with the rapidly falling costs of personal computers allowed acid house music to fill M25 fields with thousands of gurning teenagers, these same developments also allowed the digitisation of patient notes. The

recording, storage and transfer of patients blood test results, in particular became a fertile ground for product development. Early efforts, like most software at the time, were clunky and often fell over, but over time useful, easy-to-use, secure and private platforms for the management of patient data and notes came to the fore. In primary care, the EMIS's of the world started in a single GP practice in Yorkshire, and grew rapidly to manage and make sense of tens of millions of patients' clinical data – all controlled by the healthcare system and the clinicians themselves. Winners emerged and monopolies were forged. Patients were, in the main, blissfully unaware.

Fast-forward ten years and access to the web, along with a now near ubiquitous ownership of personal computers made some big companies, Microsoft and Google amongst them, ask whether the healthcare system ownership of patient data was the right way of going about things. What if patients held this same data, securely and privately, and they controlled who saw it and when? People like to be healthy, right? And they like computers? So what's not to like about having all your records in your own hands. Only they didn't, or at least they didn't like the idea enough to make it a thing. As multi-million pound health data IT programs were wound down, people were left asking whether health really could be changed by technology, or would it be the last bastion, when commerce, travel, banking and even dating had rolled-over.

"...PEOPLE WERE LEFT ASKING WHETHER HEALTH REALLY COULD BE CHANGED BY TECHNOLOGY, OR WOULD IT BE THE LAST BASTION, WHEN COMMERCE, TRAVEL, BANKING AND EVEN DATING HAD ROLLED-OVER."

Another ten years on and whilst Google licked the wounds of the now shelved Google Health (and tried to unload all the data from the patients who had used it onto Microsoft HealthVault), people kept getting poorly and in doing so they kept creating health data, either in clinics, or increasingly in their own homes using devices of all descriptions. But now they were actually carrying computers in their pockets in the form of smart phones. Always present, incredibly addictive, masterful at capturing data, and packed full of sensors that could be used in a healthcare context. eHealth became mHealth, and there was reason to believe technology could impact human health again.

THE THREE HORSEMEN

So now to round out the definitions. For the sake of simplicity, I've come down on three domains within Connected Health, into which I've grouped the main terms in use at the moment (don't worry about emailing me if you don't agree).

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TELEHEALTH/TELEMEDICINE

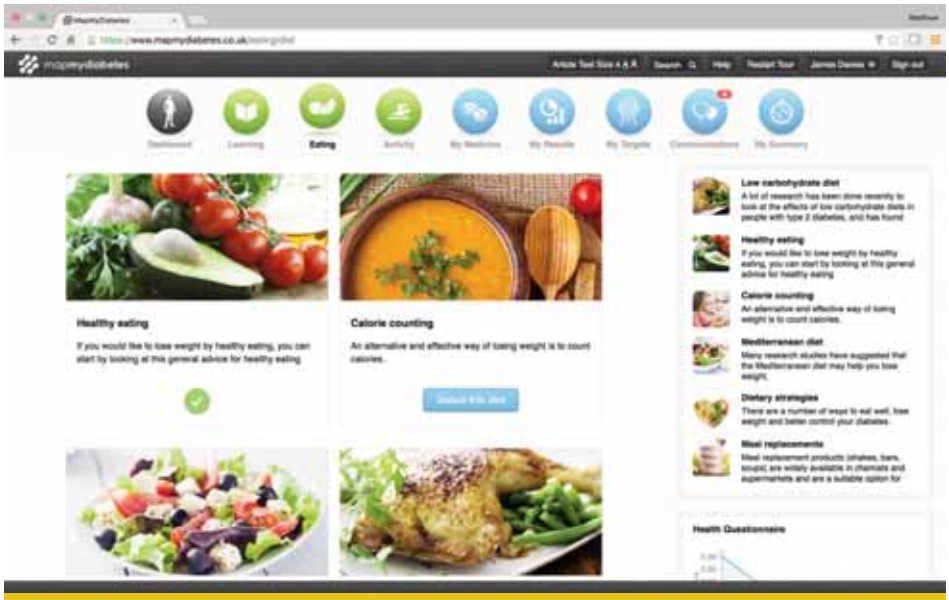
Perhaps the best known of the Connected Health care services, telehealth and telemedicine involve the use of secure portals to connect clinicians with patients in a way that is more scalable than one-clinician/one-patient, and more patient-centric than standing in-line for a GP appointment. Telemedicine (the use of real-time medical consultations using secure video links), in particular has been used effectively in the management of patients in hard to reach geographical areas. Newer, artificial intelligence supported, services such as Babylon (www.babylonhealth.com) offer this, plus a potential future solution to the scalability challenges of recruiting (and keeping hold of) clinicians. Whilst no-one is planning to replace doctors entirely just yet, the long term ambition of using AI to triage and treat the simpler cases, whilst saving human expertise for the more complicated issues could enable a scalability that would otherwise be limited as long as consultations are reliant on expensive human beings.

For completion, Telecare – the use of connected remote equipment – made famous, and then infamous by 'The Whole System Demonstrator' in the UK, is specifically used to refer to connected devices in the home. The term is increasingly being usurped by more general telehealth, using both people and devices together.

ELECTRONIC HEALTH RECORDS (EHR)

Why should GPs and Hospitals have all the fun, owning patient notes, making it difficult and even expensive for patients to access their records? Services like Patients Know Best

> "Telemedicine (the use of real-time medical co nsultations using secure video links), in particular has been used effectively in the management of patients in hard to reach geographical areas."



(www.patientsknowbest.com) offer patients a personal copy of their health record, with granular consent of data sharing, with a view that once a patient owns their own notes, the technical barriers between healthcare organisations come tumbling down…Find yourself in hospital in a strange part of the world? No problem, you have your notes in-hand already. A side benefit is the increased patient empowerment and health engagement that may come as a part of having ownership of your health record, though measurement and quantification of this is usually not a priority for such companies, who are more focused on the technical and clinical integration of their services.

DIGITAL THERAPEUTICS (THE ARTIST FORMERLY KNOWN AS MHEALTH)

Cuts in health funds and competition for budgets require enhanced efficacy and efficiency of healthcare services provision. Engaging patients in the responsible self-management of their health is widely acknowledged as a way to answer those challenges. Digital therapeutics provide those tools – purpose designed software to educate, coach and support patients in their quest for better outcomes. This domain is arguably the closest to the traditional Phama/Biotech development model, with organisations like Mapmyhealth (www.mapmyhealth.co.uk) applying the clinical development and medico-marketing model directly to software. Instead of pharmacology, think behavioural change. Instead of Phase 3, think real-world, real-time data. But both strive for the same thing – enhanced clinical outcomes, and improved cost-effectiveness. One of the attractive things here is that appropriate digital support of patients can simultaneously improve multiple parameters (HbA1c, weight, blood pressure, QoL) but is known to have a very benign safety profile. In that respect, digital therapeutics has Pharma and Biotech firmly in its sights.

THE END OF HEALTHCARE AS WE KNOW IT?

As with many industries, technology increasingly provides the tools to improve delivery to the customer (the patients), and the uptake of those technologies may precipitate a fundamental change in the way that care is consumed. As such it's easy to fall into one of two extremes – either the assumption that health and healthcare interventions in particular are too complicated to be radically altered by the rise of technology, or on the other hand feeling a nagging unease that we're all going to lose our jobs to robots (or even worse to software). The truth of course lies somewhere in between. The complexity of healthcare delivery provides some protection from the rapid industry 'disruption' that has seen a virtual end to traditional business models from record stores to taxi cabs, but all the signs are there that technology will impact patient care in a huge way in future. The question is more 'how and when', than 'if'.

WIN-WIN?

Now this is where it starts to get interesting for all of us – where the rise of technology isn't just something that may never happen, or an impending threat to the medicines model, but a direct companion to medicines both new and old. A 'Digital Robin' to 'Pharmacological Batman'. A 'Technological Burt' to 'Biological Ernie'. A new, scalable and relatively cheap way to increase efficacy, reduce the impact of side-effects and drive compliance. What's not to like?

These new software initiatives could be developed alongside medicines, and purposely designed to support the efficacy of the drug, whilst minimizing any safety or tolerability challenges. Phase 3 programmes could be shadowed by the development of digital therapeutics that buddy with the medicine in question. Phase 4 programmes would show the differences between using the medicine alone compared with medicine plus digital therapeutic.

AND FINALLY…

Connected Health involves the convergence of health technology, digital media and mobile devices and is increasingly seen as an integral part of the solution

to many of the challenges facing the healthcare sector in various areas of the world. The delay in these services becoming standard-of-care is partly due to the integration challenges at a service level, and partly due to a lack of clarity amongst decision makers on the relative benefits of these. What is not in doubt is that the quality of the technologies themselves is already more than adequate to support large-scale uptake when the time comes.

As healthcare shifts inexorably towards a patient-centred, outcome-based delivery model, Connected Health, and digital therapeutics in particular, offer an important addition to delivery, as well as a vital tool in the restructuring of services. The willingness and ability of key stakeholders on the healthcare side to embrace this as a core part of that service provision will determine the rate at which that happens. In addition the development of expertise in the

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SPECIAL FEATURE:
Healthcare

In the Age of Technology

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commissioning of novel services will need to be developed to ensure that aspiration becomes reality.

Next Issue: Companion Digital Therapeutics – finally a step 'Beyond the Pill'

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INNOVATION:
Innovation for impact

A New Way of Working for a Changing World

From Professor Steve Caddick, The Wellcome Trust

Wellcome exists to improve health for everyone by helping great ideas to thrive. We have a proud history of backing great scientists to develop their ideas from fundamental research to an impact on human health.

Wellcome is making a greater commitment than ever to innovation to help turn science and technology into inventions that will transform people's lives. Over the next five years we plan to commit up to £500m to support innovation.

OUR STRATEGY FOR INNOVATION

Through this new approach we want to help researchers and organisations across the world to transform great ideas, discoveries and inventions into treatments, products and cures for disease. Our aim is to help develop transformational technologies and to make a meaningful impact on human health.

Our past approach to Innovations has delivered remarkable success and we are going to build on those successes. But we recognise the increase in scale of complexity of the innovation landscape and the key role that Wellcome can play in supporting innovation in a changing, connected world.

OUR THREE STRATEGIC AIMS ARE:

* Building better links between science, technology and innovation by removing barriers between disciplines to make it easier to take the first translational step. We will play a more active role in supporting technology that has the capacity to enhance science and be applied to health.

* Creating a global community dedicated to innovation for impact. We will tap into our international network of companies, supporters and expert advisors to help encourage people from outside the life sciences to engage in biomedical research and innovation.

* Supporting the next generation of innovation leaders. We will work with emerging innovation leaders, giving them support and access to mentorship through interaction with our global network. We aim to encourage a greater diversity of career paths for scientists by helping them to engage in translation and innovation at an earlier stage in their career.

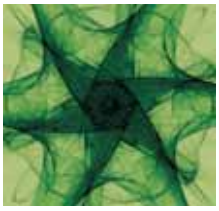
OUR APPROACH: HOW WILL WE PROVIDE SUPPORT?

We will provide support in four distinct ways, which are summarised below. We are also absolutely committed to continuing our support for existing awards to the end of their term.

STARTING WITH SCIENCE – ENCOURAGING EARLY TRANSLATION

The majority of Wellcome's funding goes into discovery science. Because Wellcome is committing even more money than ever before to science, we believe that there are greater opportunities for translating science directly into improvements in human health.

We will be contacting Wellcome-funded institutions and researchers to see how we can support early translation – through pilot / proof of concept awards.



INNOVATION:
Innovation for impact

A New Way of Working for a Changing World

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We will work closely with scientists to identify promising discoveries that have potential for translation and innovation. The Innovation team will help identify the next steps for translation, and in some cases provide small pilot awards to test feasibility.

Building for impact from our existing portfolio - from early translation to patient impact

Innovations at Wellcome has previously focused on funding the gap between academic research and commercial viability – we will continue to support such opportunities.

But making new products through a commercial route is not the only way to translate science into health. We know that clinician scientists are ideally placed to take new discoveries and insights and apply them directly into clinical practice - without necessarily requiring the development of a new product.

A broader innovation community

In February 2017 Wellcome will be launching 'Innovator Awards' for proposals of up to £500k. One of the aims of this scheme will be to encourage people that do not currently work with us to apply - including translators and innovators from outside of the life and medical science community. We think this is important because new technology has the potential to transform biomedical science, as well as have significant applications to health.

Flagship awards in order to achieve greater impact

We believe that in order to achieve greater impact on human health - we also need to focus on a smaller number of activities - something that we refer to as Flagships.

> "Our aim is to help develop transformational technologies and to make a meaningful impact on human health."

So we will diversify our approach in pursuit of clinical impact - and will seek to work with clinician scientists committed to translation. We may work later in the development path, to help provide robust scientific evidence necessary to enable implementation - be that in drug repurposing, imaging and technology innovation, digital interventions, diagnostics etc.

Our initial priority will be to ensure that our existing portfolio of projects is well supported and we will proactively identify opportunities for early impact. In a small number of cases that may mean providing additional follow-on awards for particularly promising projects.

An example of an existing Flagship is the Hilleman Laboratories – an R&D facility in New Delhi, dedicated to generating new vaccines. This is a joint venture between Wellcome and Merck, USA. We also consider our recently announced Wellcome Centres at Kings College, Dundee University and UCL as Flagships.

We will develop our Flagship activities in a flexible way - providing the resources necessary to ensure that we maximise impact from a partnership. Some will be used to support early translation, some later to drive to

impact. Because these will be particularly significant investments we are taking some more time to develop our approach. We do not expect to have more than 20 Flagships over the next five years.

OUR GOALS AND PRIORITIES

We care about impact in the immediate term and expect that by 2022 we will have supported interventions that improve the lives of at least 1 million people per annum. In addition, we will develop a portfolio of activities that deliver impact in 5 years - but with the potential to deliver longer and even greater impact on science and in health over the following 10-20+ years.

We will remain open to great ideas in any area. In our first year much of our support will focus on ideas and solutions involving mental health, neurological disorders and neglected tropical diseases, but these are not exclusive and other areas of particular interest will be announced in the future.

We will revisit, refine and change our themes and expect to have further themes in due course.

Independent, expert peer review will continue to be central to our decision-making - especially to help determine scientific quality and technical feasibility of proposals. But we will also complement peer review with further analysis and due diligence depending on the scale of investment proposed. For larger investments, key elements will include: value for money, deliverability, patient benefit and project / team resilience.

SUMMARY

We are grateful to all of you - our friends, collaborators, partners, advisors and supporters - for all your help to get us to this exciting position. We are at the beginning of an exciting new era for Innovation at Wellcome. We look forward to working with the global community to embrace new approaches, new technologies and new ideas – for a single purpose – to improve human health.

We want to help researchers and organisations across the world to transform great ideas, discoveries and inventions into treatments, products and cures for disease. If you have an idea that you think could advance science and improve health, and believe that Wellcome can help you deliver impact please email innovations@wellcome.ac.uk.

Professor Steve Caddick, Director of Innovation

RETRO FEATURE:
Biosimilars:
Are the non-identical twins of Biopharmaceuticals safe?

By Dr Matthew Hickling who was Medical Advisor at UCB at the time of first publication.

This article was first published in PP in May 2010. Given the recent successes in the registration of biosimilars, it bears re-reading and further consideration today.

Matthew Hickling

INTRODUCTION

BIOSIMILARS (GENERIC OR follow-on biopharmaceuticals) are a growing consideration for the pharmaceutical industry and possibly offer cost-effective alternatives to branded counterparts for payers and prescribers[1], a large market given that the sale of generics accounts for up to 50-70% of all 'Prescription only medication' sales in some countries[2]. With recent and future patent expirations for a number of biopharmaceuticals, one might therefore expect an explosion in Biosimilars. However there are a number of critical safety considerations that could impact on the potential success of Biosimilars, particularly relating to their specific protein structure and immunogenicity as well as consistency in manufacture.

A generic must demonstrate bioequivalence to the reference medicinal product in patients with a specific condition in a given formulation[3]. Chemically synthesised small molecule drugs or NCEs can be relatively easy to characterise and established abbreviated approval pathways have enabled their adoption, often resulting in significant drops in costs to payers[4]. Unlike NCEs, Biosimilars are not considered 'identical' to the original biopharmaceutical; hence the adoption of the terminology 'Biosimilar' rather than 'Biogeneric'[5]. Regulatory authorities and biopharmaceutical companies have therefore encountered obstacles in devising a clear route for their introduction. This article will outline some of these concerns for Biosimilar adoption.

DO YOU ADD SUGAR?

Whereas NCEs can easily be synthesised and purified with high a degree of certainty, biopharmaceuticals are generally large complex proteins (100-1000 x NCE) that depend upon the maintenance of the tertiary or quaternary structure for biological activity, often a product of post-translational modification (PTM)[6]. PTM may however also increase the potential likelihood of immunogenecity, a major safety concern for biopharmaceuticals[7].

Protein glycosylation forms a major part of PTM in over 50% of human proteins, the process by which this occurs and the consequential effects are only partly understood. Recombinant human erythropoietin (rhEPO), monoclonal antibodies (mAbs), some growth hormones as well as some clotting factors all require glycosylation to ensure biological activity. Glycosylation is however a very heterogeneous process, with different sugars potentially being added to the proteins whilst passing through the Golgi apparatus depending upon on the manufacturers favoured cell line. Other PTM processes include carboxylation, hydroxylation, sulphation and amidation, all of which play an important role in influencing the final conformational shape of proteins and therefore their functional activity and safety.

One example highlighting the importance of PTM on changing a proteins profile is seen with rhEPO. This biopharmaceutical is administered in the treatment of various causes of anaemia[8]. Carbohydrate residues comprise up to 40% of the total molecular weight of rhEPO; the subsequent alteration in type and position of the residues leads to

different isoforms, changes in thermal stability as well as differing aggregate formation properties[9]. Single amino-acid site directed mutagenesis studies have demonstrated a dramatic loss of in-vivo activity attributed to the reduction in the elimination half-life through increased renal clearance of the mutated aglycosylated rhEPO[4]. The efficacy of biopharmaceuticals such as mAbs is also affected by glycosylation through the differing recruitment patterns of different activators of Antibody Dependent Cellular Cytotoxicity (ADCC)[7].

Cell lines used by different companies for protein expression systems are rarely the same, the implication being that biopharmaceuticals cannot be exactly copied[10]. The consequence of a particular pattern of PTM upon the biological function of a biopharmaceutical cannot also be fully appreciated prior to preclinical testing, and even then, the effect may not be fully understood until extensive clinical trials are conducted. Therefore how similar should the PTM profile of the Biosimilar be compared to the original biopharmaceutical, and is it possible to manufacture and assess?

> "BIOPHARMACEUTICALS CANNOT BE EXACTLY COPIED"

THE POTENTIAL FOR IMMUNOGENICITY AND PROBLEMS IN MANUFACTURING

PTM appear to play an important role in determining immunogenicity and without fully understanding the processes that are involved, slight differences in the PTM profiles of biopharmaceuticals could increase the immunogenic potential. Escherichia coli based expression systems lack the ability to glycosylate, and this has been linked to an increased risk of immunogenicity for some proteins (but not all), through the exposure of different epitopes, often masked in the endogenous glycosylated version[11]. Glycosylation can also be altered by the manufacturing conditions through changes in pH, nutrient and metabolic by-products as well as the presence/absence of cytokines and hormones[4].

Small changes in any step from the cell line selection for the protein expression system, through to the administration of the final product to the patient can make a major difference to the potential for an adverse drug event i.e. two similar biopharmaceuticals could not only vary in their efficacy but also stimulate two different immunological responses[10]. Even the method of administration has been shown to alter the immunogenic potential, with intravenous administration possibly conferring a lower risk than intramuscular or subcutaneous injection[12]. One must also consider the presence of impurities, aggregates, the final formulation profile as well as the intended means of storage, as all have been shown to potentially increase the risk of immunogenicity and therefore result in the loss of efficacy and affect safety. Even the slightest of changes in the manufacturing process can lead to dramatic and severe adverse drug events, as seen in the case of epoetin-α; a minor change in the manufacturing process resulted in a rare but catastrophic series of adverse drug reactions, caused by the formation of antibodies to both the product and the endogenous erythropoietin that resulted in a pure red cell aplasia (PRCA)[5, 6]. Although the exact cause is still not clear, one possible explanation is the formation of antibodies following a formulation change where human serum albumin was replaced with glycine and polysorbate 80 that may have subsequently acted as an adjuvant[5].

Whilst numerous biopharmaceuticals induce an immune response, not all are clinically significant, and even when significant, they can still be quite rare. The incidence of PRCA in the use of epoetin-α was estimated to be 18 per 100,000 patient years with a 9 month median duration of treatment before detection[13], illustrating how difficult the detection of immune mediated adverse drug reactions can be. Whilst it is very difficult to predict whether a biopharmaceutical will induce a clinically significant immune response, effective pharmacovigilance is made infinitely more difficult when the incidence is so low. With a multitude of variabilities which include a number

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Biosimilars:

Are the non-identical twins of Biopharmaceuticals safe?

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of patient related factors that impact upon the potential immunogenicity of a Biosimilar, it is difficult to imagine how the detection of an antibody mediated adverse drug reaction resulting from treatment with a Biosimilar could be detected without thorough post marketing pharmacovigilance.

TRUST IN THE QUALITY OF THE PRODUCT

A major criterion for ensuring patient safety is comparability between batches of either any product, whether original biopharmaceutical or Biosimilar. Every batch should contain product with identical (or near identical) physicochemical characteristics so that the pharmacokinetic and pharmacodynamic profile can be assured. To satisfy this, a number of analytical tests are required, often leading to fresh challenges. It can be difficult to fully characterise the subtle PTM changes in structure of these high molecular weight, complex glycoproteins, leading to undetectable changes in product profile[14]. There is also a lack of universal standardisation of analytical tests between laboratories, hindering reproducibility[15]. This is further complicated by the fact that immunogenicity takes time to develop; an extended period of exposure to the biopharmaceutical may therefore be required[16]. The fact that the mere detection of an immunogenic reaction doesn't always result in an antibody mediated adverse drug reaction adds further complexity, especially as the sensitivity and specificity of some analytical tests may result in a number of false negative/positive results[18].

Ensuring comparability can prove difficult especially when the manufacturing process is changed or moved to a new location. Studies have examined batches of different preparations of biopharmaceuticals that contain distinct mixes of isoforms comprising many different glycosylation patterns[17, 18]. Heterogeneity between batches of identical preparations has also been shown[19]. The immensity of the problem of ensuring comparability between batches of a biopharmaceutical as well as similarity between an original and a Biosimilar is represented by the number of analytical tests required during the manufacturer of interferon-α-2a; over 240 tests were used in this process[14]. Regulatory authorization is therefore required when any change to the manufacturing process is made, often requiring preclinical and clinical data confirming bioequivalency to the original product.

In summary, it can be seen that the process of merely copying an original biopharmaceutical to produce a cheaper and bioequivalent Biosimilar, without increasing the risk of an adverse drug reaction is at least complicated if not uncertain. With a long list of plausible problems in designing the approval process, guidelines for Biosimilars have been published in the European Community[20, 21], whilst definitive guidance is still awaiting approval in the United States. A number of difficult questions regarding how much safety and bioequivalence data are required are still being asked, further complicated by intense lobbying from interested parties in the biopharmaceutical industry.

The EMEA together with the Committee for Human Medicinal Products (CHMP) have devised guidelines for the preclinical and clinical evaluation of Biosimilars that were published in 2005[20] and 2006[21]. Following the publication of these guidelines, they have been subsequently tested with some approvals and rejections[16]. Although the clinical assessment of Biosimilars is less substantial than for the original biopharmaceutical, it is imperative that the issues of quality, safety and efficacy of the Biosimilar are addressed before authorization is given, the level of which should be made on a case by case basis, taking into consideration the complexity of the Biosimilar.

Pharmacovigilance surveillance is an integral part of the monitoring of

biopharmaceuticals after approval. However given the uncertainty of the validity of preclinical testing, as well as the lack of certainty of clinical trials detecting rare immune mediated adverse drug events, lengthy pharmacovigilance surveillance may be required.

Within the United States, there are currently no formal guidelines or current legislation that enables the approval of Biosimilars. Within the Abbreviated New Drugs Act[22], there is no allowance for the licence of biologics, normally covered by a Biological Licensing Application under the remit of the Public Health Service Act as well as the Federal Food, Drug, and Cosmetic Act[23]. NCE generics do not normally have to include preclinical or clinical data on safety and effectiveness, the requirement is that they need to only demonstrate bioequivalence in the form of comparability in dosage, form, administration, quality, performance and intended use[22].

> "THE PROCESS OF MERELY COPYING AN ORIGINAL BIOPHARMACEUTICAL TO PRODUCE A CHEAPER AND BIOEQUIVALENT BIOSIMILAR, WITHOUT INCREASING THE RISK OF AN ADVERSE DRUG REACTION IS AT LEAST COMPLICATED IF NOT UNCERTAIN."

Whilst the approval pathway for Biosimilars has yet to be determined in the United States, there are a number of bills which are being currently proposed[24]. These bills outline periods of exclusivity that range from 5 to 12 years for new products with 3 to 14 years from new indications; all agree on an additional 6 months for paediatric applications. There is still some debate on the outcome of these bills and how they will impact this growing sector.

CAN THEY BE SUBSTITUTED?

There is a continued debate over whether substitution of one Biosimilar for another, or replacement for an original biopharmaceutical should be allowed. The argument against substitution is based upon the uncertainty of similarity between biopharmaceuticals, given the concerns over the difficulties in fully characterising and comparing these complex proteins. Substitution if allowed would have to be conducted with some caution; the prescriber would have to ensure that they fully understood the potential differences between the two products. Although the regulators have not issued guidance to prevent substitution, legislation has been passed in France and Spain disallowing substitution[2]. If further legislation is passed in other countries, this could provide an additional barrier to adoption of treatment of existing patients with Biosimilars.

NAMING IS IMPORTANT

All drugs are assigned a name under the International Non-proprietary Name (INN) system which was originally developed for NCE for the identification of unique and individually pharmaceutically active substances[10]. Traditionally drugs were only given the same name if they could be proven to be analytically identical with corresponding identical biological activities. There is an ongoing debate on whether Biosimilars are similar enough to warrant the same name. Those with vested interests in generics believe that there is sufficient evidence to demonstrate comparability to assign the same INN; strongly contested by others who believe that different INN names are essential in protecting patients by allowing effective pharmacovigilance[20]. Although assigning different names may help distinguish a Biosimilar from an original biopharmaceutical, this has not occurred with the first generation of biopharmaceuticals used for the replacement of hormones and clotting factors[10]. INN name changes have also not been required when changes in the manufacturing process have caused subtle changes in the final product[10].

HOW DO WE ENSURE THE SAFETY OF BIOSIMILARS?

Other strategies could be used to ensure patient safety and the maintenance of effective pharmacovigilance. Firstly, Biosimilars could be given quite distinctively different brand names so that they could not be confused with an original biopharmaceutical, therefore preventing inadvertent substitution[10]. Secondly, statements that highlight the issues of substitution as well as potential differences between Biosimilars and original biopharmaceuticals could be included within the 'Summary of Product Characteristics'[10]. An electronic bar-code system could be introduced to ensure that potential adverse drug

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reactions are appropriately assigned to the correct POM, enabling more effective pharmacovigilance[10].

CONCLUSION

The emerging market for Biosimilars is potentially lucrative (with therefore hotly contested and strongly held bipartisan views) however there is a range of opinion on how rapidly this new class of therapeutics might expand. On one hand, the introduction of Biosimilars potentially offers biopharmaceutical therapeutics at 'cut down prices' that are 'at least as effective' (not necessarily better and cheaper, might be only 'as effective' as their original counterparts). This would open up fiscally restricted markets, enabling health care providers to offer more treatment options within shrinking budgets, benefiting more patients where funding is difficult. However the safety and reliability of Biosimilars has also been strongly contested with numerous incidences of adverse drug reactions caused by problems in PTM or manufacturing. The developments in legislation and formal guidance over the next few years may well determine the outcome for this pursuit of cheaper, more effective therapies.

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COFFEE BREAK:
The Art of Company Committeeship

by Katie L. Chain MS (a nom de plume)

KATIE GIVES EXPERIENCED GUIDANCE HOW TO SUCCEED IN MEETINGS

"THE WORLD IS run by those who show up" How true. In my time I have had wall-to-wall, back-to-back, 9-to-5 meetings that have squeezed out any chance of doing any real work that day... and the next. Tempted to give it a miss? Just try and you will find you have lost a platinum opportunity to shine, have been volunteered to head up the project from hell, and earmarked as "disappointing" (i.e. career limited) by the chairman. Sounds familiar? So, how DO you succeed at meetings? Katie gives the unseasoned wage slave some tips below:-

ARRIVAL

1. Never arrive on time. That shows you are too eager and a beginner. Arrive a little late, slightly out of breath and clutching a handful of papers with lots of numbers and graphs on (that is important, as you will see later). Give brief apologies to all and the chairperson (by name to them), saying words to the effect you have just been in another meeting/telecom/videocom that saved a media storm/avoided an ABPI Code compliant/ resuscitated the company cat [delete as appropriate].

2. NEVER ARRIVE WITH COFFEE AND/OR A BACON SANDWICH – that will blow your cover.

3. Dress to not be noticed. That means, blend in. This is not a good time for Jimmy Choo shoes or a Louis Vuitton hand bag; neither is an undersized Sex Pistols vintage tee shirt you had 20 years ago.

THE AGENDA

1. The chances are you have not read the agenda. Unless you are very unlucky (or have an enemy in the room), you will not have "outstanding actions" or an agenda item against your name. Even so, try to say nothing until the meeting is at least half over. This gives you time to read the agenda (which you should do without being noticed). It will also allow you to see who are the power players, who are the lambs to the slaughter, and how best to contribute. Your silence will also give you the appearance of listening (which people like) and an air of respectful wisdom.

2. Nod at people when they speak and make a note. That shows you value their contribution and gives you a chance to note to buy some wine on the way home.

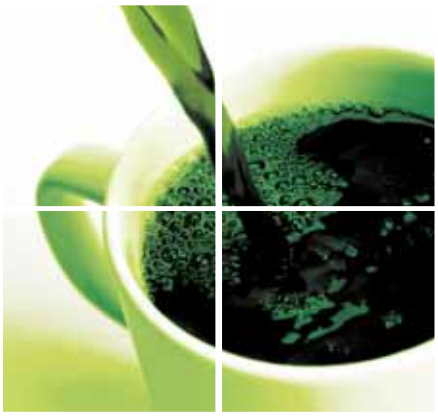
3. If asked a question, be as vague as possible. This has three key benefits:

a. It avoids irritating those with strong opinions

b. It keeps your options open until later when might have to side with a power player

c. You cannot be wrong

4. If you feel moved to contribute – don't. You are reacting and that smacks of emotion (usually anger or frustration). You will likely say something that is going to get you an "Action" in the minutes. You should know that to succeed in a meeting you must enter and leave a meeting with no "Actions" to do or be done by you.



5. Choose your moment to speak, best done when there is a hiatus in discussion (which usually means people have run out of ideas.) Now is the time to pick up those papers (with lots of numbers and graphs on) in a way that implies you have some data on the topic at hand. If asked to see these data, polite reply these data are "immature" at the moment and needs further work. NEVER LET THEM SEE THE PAPERS (which you borrowed from your mate, the canteen manager, about the vegetable invoices from the wholesaler).

6. When speaking (if you have to) repeat the occasional buzzwords others have used. But do, please, use term in context – "Yes, I had a rationality but the wheels fell off" isn't going to work.

7. Like the Royal's credo –"Don't explain and don't complain". In fact, just…. don't do anything, if you can.

ACTIONS

1. I will repeat myself here - to succeed in a meeting you must enter and leave with no "Actions" to do or be done by you.

2. If you are in an unfortunate position of being perceived as an expert or, even worse "the right man for the job" (especially irritating if you are not a man), there is only one route you can take – suggest a "Subcommittee" be formed. That demonstrates you are truly a "committee man" (groan again) to the assembled rabble but avoids you personally coming up with any ideas. Indeed, any outputs that do not meet with the main meeting's approval can be blamed on the Subcommittee, not you. If cornered into chairing the subcommittee, you - the chairperson (thank you) – should know the power of …delegation.

BE POPULAR

1. If you really must turn up on time (train arrived early) bring chocolates and snacks to share. At least it means that you get something to eat.

2. Suggesting coffee breaks (even if scheduled in the agenda already) will make you popular. However, never leave a meeting early for any reason – that makes those that are left in the room feel unimportant and envious of your escape. Hate will follow. The correct ploy is to suggest an early adjournment. This is what everyone was hoping for. Give credible reasons e.g. there is insufficient time to cover all the important agenda items/there are complex issues that might need further expert input/the fire alarm has gone off.

DID YOU SUCCEED?

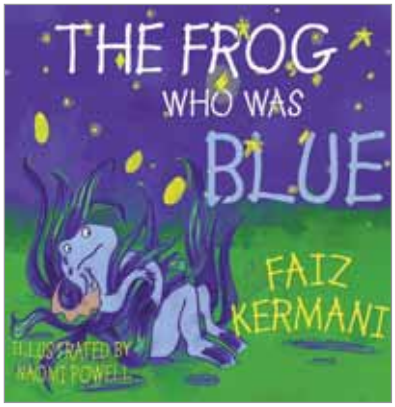
Succeeding in committeeship (as with any project) requires goals, objectives, strategies and tactics, critical success factors, milestones, and endpoints. For the successful meeting person (you) there is only one endpoint - you got home in time to buy and enjoy that bottle of wine.

THE FROG WHO WAS BLUE

Dr Faiz Kermani

Matador
ISBN: 9781785899959
Price: £6.99

COULD DR FAIZ Kermani be the only person in the world who has published both on clinical trials and on frogs? He hopes so!



I was surprised to be asked to review this children's book for "Pharmaceutical Physician" until I realised that any money raised from sales will go to support mobile children's health clinics in Malawi, run by the World Medical Fund.

I initially trialled the book while babysitting, with a tricky pair of two and four year- old boys who don't particularly like reading or bedtime stories. -It has become a bit of a chore for them, instead of the lovely time I remember with my own children.

They were entranced by the excellent and irreverent, brightly coloured illustrations and the great use of names which really caught their imagination. Good. Now we've settled down and can read the story together. As with most books aimed at the pre-school child, the book is text light and picture heavy. (Which is also a boon to exhausted parents longing for winoclock.) We romped through the simple but effective story about Biriwita, a lonely blue frog who longs to be accepted at Croak College, the most famous school for frogs in Malawi. However, they all turn their backs on him as he is just too different... "What's wrong with you? Why are you blue? You're the strangest frog we've seen. Normal frogs are green!"

In scenes of high drama involving a crocodile and a rock, Biriwita comes into his own and saves the day. Nobody cared that he was blue anymore: he was a frog. And the story ends happily ever after with a party. The book passed the 'read it again' test without me getting completely fed up with it and the boys happily making accompanying frog noises and generally enjoying the plot.

Do girls like it? Yes, very much: but interestingly the random sample of two five year olds who had started school in September brought a slightly different reaction, talking about how it felt to be new to school for outsiders before everyone settled in.

Key themes for children today about acceptance, fitting in and moving nurseries or schools captured very cleverly by an accomplished author. And I do like a happy ending.

Jenna Lucas

Editor: An unashamed plug - buy the book – the money will help to pay for paediatric clinics in Malawi - and it is good fun.

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NEW MEDREGS BLOG

MHRA HAS LAUNCHED AN OFFICIAL BLOG PROVIDING EXPERT INSIGHT INTO THE LATEST REGULATORY THINKING AND ALL ASPECTS OF MEDICINES REGULATION. (FEBRUARY 2017.)

IF YOU'RE WORKINg to develop and submit applications to MHRA for marketing authorisations and clinical trial authorisations, then you need to keep up to date with the latest regulatory thinking and be able to easily avoid common pitfalls.

Visit the MedRegs blog

Our blog will feature posts from experts who work right across the regulatory process. They'll share their top insights and experience on a range of topics to help you stay informed, engage with our processes more effectively, and find out more about what we do to protect public health

We will be covering topics such as:

- submissions – how to get them right first time
- behind the scenes – find out more about how the regulator works
- key issues – the inside track on emerging issues for the regulation of medicines

Dr Siu Ping Lam, Director of Licensing, MHRA said:

Our MedRegs blog is another opportunity for us to connect directly with our stakeholders and customers in a less formal way, help them avoid common and easily avoidable errors and engage with us on issues that are important to them.

It also offers them an opportunity to share their thoughts and comments with us, and will encourage further two-way conversation between our regulatory specialists at MHRA and those working across industry, academia and healthcare.

We'd like to know what you think about our posts, so we can develop a really useful and informative blog. Let us know if you have ideas about what would be useful for us to cover.

Sign up to get new post alerts

Look us up on *Facebook, LinkedIn,* or *@MHRAgovuk* on Twitter

PARTNERSHIP TO PROTECT PUBLIC HEALTH – MHRA AND HTA SIGN AGREEMENT

THE MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA) AND THE HUMAN TISSUE AUTHORITY (HTA) SIGNED A PARTNERSHIP AGREEMENT IN DECEMBER 2016.

Working in an increasingly innovative environment, regulatory authorities must balance their essential roles in protecting public health with making

sure new, innovative treatments are made available to the UK healthcare sector at the earliest, safest opportunity.

To support these responsibilities, and their ongoing working relationship, the Human Tissue Authority (HTA) and the Medicines and Healthcare products Regulatory Agency (MHRA) have signed a partnership agreement; strengthening a collaboration which began in 2005.

This agreement covers the work of the HTA as the regulator for the safe removal, use and disposal of human tissue and organs in the UK, and of MHRA as responsible for regulating all medicines, medical devices and blood components for transfusion in the UK by ensuring they are acceptably safe and to support the innovation and new products being brought speedily and safely to patients.

The agreement promotes further collaboration and strengthens the commitment to working together for the benefit of patients, staff and stakeholders and to enhance regulation.

The main areas of cooperation are joint advice through the 'One Stop Shop' regulatory advice service for regenerative medicine (RASRM), joint inspections of Tissue Establishments and advanced therapy medicinal product (ATMP) manufacturing sites, and a joint position on the use of blood for ATMP manufacture.

Strengthened collaboration between the HTA and MHRA will contribute to a supportive approach to innovators in the development of new products and services. The agreement will also enable a reciprocal arrangement between the agencies to use investigational knowledge and experience.

MHRA Chief Executive Dr Ian Hudson said:

"Our commitment to protecting the health of UK people is aided by creating close ties with regulatory counterparts. Working together we will be better able to identify, develop, and support transformative innovations in the UK healthcare sector.

Agreements such as these help to further strengthen our ability to promote good practices and we look forward to working even closer with the HTA."

HTA Chief Executive, Allan Marriott-Smith said:

"We welcome this agreement as it strengthens our commitment to collaboration for the benefit of patients, staff and stakeholders. By working together, we are able to streamline and simplify the regulatory environment for those we regulate.

A more collaborative approach to regulation will help us ensure our approach to licensing and inspection is proportionate and efficient. It will also enable us to further support innovation while continuing to ensure that human tissue is used safely, ethically and with proper consent.

We look forward to continuing to work closely with the MHRA."

OHE is Pleased to Announce the Appointment of Two New Economists: Margherita Neri and Jimena Ferraro

Margherita Neri

Margherita Neri joined the OHE team in December 2016 following completion of her MSc in Economics at University College London. She also holds an undergraduate degree in Economics and Statistics from the University of Siena, Italy, which included a year spent as a visiting student at the University of Oxford.

Margherita Neri

Margherita's research interests focus on the evaluation of healthcare policies, including incentives to optimise the demand and supply of health care as well as aspects of competition in healthcare and pharmaceutical markets.

As part of her MSc dissertation, she led an empirical study on the effect of a health care policy that introduced higher out-of-pocket prices for outpatient care services supplied by public health care facilities in Italy. Contrarily to theoretical expectations, this analysis found no evidence of a significantly negative demand response to more expensive services. Although public health does not seem particularly at risk as a consequence of this health care policy, the evidence is suggestive of the fact that access to public health care in Italy is increasingly based on the ability to pay rather than actual health needs of the population.

Jimena Ferraro

Jimena Ferraro joined OHE in January 2017. Prior to this Jimena worked as a consultant in Argentina, working across a variety of sectors ranging from regulation and competition policy to microfinance and export promotion.

Jimena's current research interests include industrial organisation, competition policy, regulation, and health economics. She has carried out research to study different competitive environments and their effects on market structures, including cheating behaviours in auctions, and strategies to

Jimena Ferraro

reduce piracy in online markets. She also conducted quantitative and qualitative research to analyse physicians' (non-monetary) incentives to do cesarean section deliveries in Argentina.

Jimena holds a PhD in Economics from the Toulouse School of Economics, where she specialised in Industrial Organisation. She spent the last year of her PhD as a visiting researcher at Imperial College Business School.