

JFPM

Edition 2

May 18

GDPR: A Topical subject - privacy and security of clinical data  
What is real world data? An introduction to the definitions used, sources of data and potential uses  
My life in Pharmaceutical Medicine by Alastair Benbow  
Engaging with the pharmaceutical industry and what this means for clinicians  
Book review: the Emperor of all Maladies

# the **JOURNAL** of the Faculty of Pharmaceutical Medicine



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## Hot topics in pharmaceutical medicine

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Faculty of  
**Pharmaceutical  
Medicine**

*Advancing the science and practice of pharmaceutical medicine  
for the benefit of the public*

# Journal of the Faculty of Pharmaceutical Medicine

Edition 2  
May 2018

*Hot topics in  
pharmaceutical  
medicine*

## Welcome!

Welcome to the new *Journal of the Faculty of Pharmaceutical Medicine*. The JFPM will be a biannual publication covering all aspects of pharmaceutical medicine and providing updates from all areas of the FPM, and news and events. Each edition will have a main theme, with contributions from FPM members, staff and external guest authors.

In this inaugural edition we review some of the current hot topics in pharmaceutical medicine, from a variety of perspectives, including: the FPM Real World Data working group give a fascinating overview of this exciting field; our incoming President, Prof Tim Higenbottam, gives his view on the impact of GDPR on pharmaceutical medicine; and the Chair of the FPM Policy and Communications Group, Dr Gillies O'Bryan-Tear, reports from the 5th Annual meeting of the Stratified Medicine Network.



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# PRESIDENT'S MESSAGE



Welcome to the first full edition of *The Journal of the Faculty of Pharmaceutical Medicine (JFPM)*.

During my Presidency of the FPM, one of my objectives has been to ensure that members receive recognisable benefits from their membership, and participate in the FPM's activities. The new *JFPM* has been developed by the Policy and Communications Group, and is a result of the review of the membership offerings that the FPM provides and is part of our initiatives to increase communications with the membership and to put educational programmes and events in place that should be of benefit and interest to all.

Our first full edition is all about current 'Hot Topics' in Pharmaceutical Medicine. The articles that are included have a strong focus on the future of our specialty and how the changes that are happening will ultimately have an impact on the work that we do as pharmaceutical physicians. Good examples are the articles on Real World Data and Pharmacogenetics and Stratified Medicine. These two topics have been talked about for a few years now and are becoming reality. These changes will have a direct influence on how we develop medicines in the future and, subsequently, support them as approved products for use by patients.

There are also items about events that we will be holding at the FPM over the coming months and again these are focusing on topics which are directly relevant to our specialty and our future working activities. The Faculty Education Day 'Applying ethical values and good practice in pharmaceutical medicine – debate / learn / develop' is on the 12<sup>th</sup> June and promises to be a great event for all those involved in education and training in our specialty, and anyone with an interest in ethical issues in pharmaceutical medicine.

Also of note is the Innovation in Medicine 2018: RCP annual conference on the 25<sup>th</sup> to 26<sup>th</sup> June. This is being organised as part of the 500<sup>th</sup> Anniversary Celebrations that the RCP are having throughout this year and is focusing on how we will be treating patients in future. The topics that will be covered are exciting and will be of interest and very relevant to us all as pharmaceutical physicians. The FPM will have a presence at the conference and I am also chairing one of the sessions called 'The Future of Medicines: what treatments will we be using in 30 years' time?'. The conference has a great line up of international speakers.

I would encourage everyone to consider attending these events if you can, so that you can stay updated and aware of the future developments in our field, become better informed about what you might get involved with in the future in developing and utilising these new approaches for the benefit of patients, and encourage you to challenge the boundaries of modern medicine.

I do hope that you enjoy reading this first full edition of our new journal. Please do let us know what you think about it and possibly consider contributing in future. The next edition will focus on paediatric medicines development – we would be very grateful for your ideas for articles and other content – fill in the form on the back page.



*Real World Data and Pharmacogenetics and Stratified Medicine. These two topics have been talked about for a few years now and are becoming reality. These changes will have a direct influence on how we develop medicines in the future and, subsequently, support them as approved products for use by patients.*

# FPM Education Day 2018

## Applying ethical values and good practice in pharmaceutical medicine

Debate | Learn | Develop



#FPMeduDay2018

### Programme

**09:00 – 09:45** **Breakfast briefing on the Diploma in Pharmaceutical Medicine exam and the trainee e-portfolio**

**09:30 – 09:55** **Registration**

**10:00 – 10:05** **Welcome and housekeeping**  
*Dr Alastair Benbow, Chairperson, FPM Ethics and Practice Committee*

**10:05 – 10.45** **A Hitchhiker's Guide to the ethical universe**  
*Professor Alan Cribb, Professor of Bioethics and Education, King's College London*

**10.45 – 11.25** **Thinking about ethical issues**  
*Philippa Foster Back CBE, Director of the Institute of Business Ethics*

**11:25 – 11:40** **Tea and coffee break\***

**11.45 – 13:10** **Workshops (first round)**

**13:15 – 14:15** **Lunch\***

**14:20 – 15:45** **Workshops (second round)**

**15.45 – 16.00** **Round-up and close**

*\*Refreshments are provided throughout the day*

### Workshops

#### Emerging issues in pharmaceutical medicine

Press reports about the 'unscrupulous' pharmaceutical industry raising prices suddenly on sick patients has raised questions about the ethics of pharmaceutical prices.

This workshop will provide attendees with the basics of the ethics surrounding pricing and reimbursement. It will also explore the impact of markets on contentious issues such as rationing, precision medicine, and the levers used to encourage companies to develop pharmaceuticals in therapeutic areas traditionally considered not profitable.

*Facilitator: Dr Tony Lockett*

#### Integrity and safety in drug development

Drug development requires careful ethical judgement. In this workshop we will use case studies to discuss seven essential principles that can help guide your thinking on R&D ethics. We will then have a closer look at risk-benefit analysis. Exploring this through worked examples, we will look at different ways of assessing risk. At the end of the session participants will have a structure to think about risk assessment and the broader ethics of drug development.

*Facilitators: Dr Josh Brostoff and Dr Alastair Benbow*

#### Morality and the Code: An approach to proactive decision-making

This workshop will consider the current promotional operating paradigm, based as it is around compliance with the ABPI Code of Practice, and propose ways business decision-making would benefit from a greater understanding and application of ethical principles.

*Facilitator: Dr Nick Broughton*

#### Standing your ground on professional values

The focus of this workshop is assertively communicating our position when an ethical conflict exists. Working with scenarios and role-play, delegates will apply a simple framework to identify conflicting values and apply Good Medical Practice to reach and communicate their position to others. Content will primarily centre around conflicts arising from commercial imperatives, professional medical values and patient wellbeing including safety considerations.

*Facilitators: Dr Liz Clark and Richard Reid, Founder, Senior Executive Coach and Trainer, Pinnacle*

**The FPM Education Day is sponsored by:**



**Date:** 12th June 2018 | **Venue:** NCVO, 8 All Saints Street, London, N1 9RL

**Registration fees:** PMST rate: £90 | FPM members: £130 | Non-members: £175

**Closing date for bookings:** Monday 4 June at 17:00

**BOOK**

# PHARMACEUTICAL MEDICINE – QUO VADIS? A PERSONAL(ISED) PERSPECTIVE

DR STUART DOLLOW

HEAD, GLOBAL CLINICAL DEVELOPMENT AND MEDICAL AFFAIRS - UCB  
AUTHORITY MEMBER - HUMAN TISSUE AUTHORITY  
BOARD MEMBER - FACULTY OF PHARMACEUTICAL MEDICINE



Pharmaceutical Medicine is a broad discipline, from first-in-man studies and translational medicine, through to pharmacovigilance and regulatory oversight for mature medicines, including generics and biosimilars. This encompasses clinical pharmacology, clinical development and medical affairs, as well as an understanding of the patient and regulatory relevance of pre-clinical research and manufacturing quality. With such diversity, it is difficult to predict the future for our specialty.

Nevertheless, it is important that we remember the principles that define pharmaceutical medicine, to guide us to more effectively shape its direction and that of the organisations and environment in which we work. These principles are founded in our understanding of patients, their diseases and the balancing of benefits and risks. As we gaze into the future these should remain foundational but not limiting, as personalised (or precision) medicine increasingly moves us away from the aggregated population approach that has been our focus.

Traditionally we have dealt in population probabilities, examining means, medians and confidence intervals that determine the benefit:risk for our selected clinical trial populations. We have always known, however, that clinical reality is different and that there is a range of patient responses that are not generally predictable at an individual patient level. This leaves an element of uncertainty for prescribers and patients to know whether they will respond or suffer adverse events. While we know these variations are based on genetic and environmental factors, our ability to predict these has been poor (with the exception of where a specific gene, receptor or polymorphism is related to a mechanism of action or denotes a marker of response).

Moving to a personalised approach changes the nature of the development of medicines and their use, as well as changing the relationship between patients and their medicines. Increased scientific rigour is needed to be able to interpret benefits and risks based upon smaller but perhaps more targeted sample sizes, as we redefine our model from a prevalence-based methodology, to one that is targeted to better predict individual success or failure with greater accuracy. With improved

pharmacodynamic / pharmacokinetic relationship modelling we are already filling some of these gaps, building an understanding of which patient factors impact the likelihood of patients to respond and, to some extent, why.

For this to become reality for more patients requires a wider change in how we discover, develop, regulate and utilise our medicines. Whether this starts with a better understanding of the nature and the impact of a given disease, or is based upon analyses of discrete differences in responses in clinical trials, it requires us to remind ourselves of the times we were treating patients. While our decisions were (mostly) evidence based, we made choices based on what we believed was best for each individual.

The increasing use of electronic health records (EHRs), wearables and health apps, improves the utility and richness of clinical data. With the advent of Artificial Intelligence (AI) we should expect prescribers to increasingly personalise therapies for individuals, and for payers to only pay for them based on the quality of the individual's outcome. Similarly, they will expect us to guide them, directly or via AI, with ever more individualised tools to diagnose, manage, treat and monitor, that will allow patients, prescribers and payers to use our medicines with increasing confidence. Thus, minimising cost and waste.



With the advent of blockchain EHRs, this will become increasingly feasible for outcomes monitoring as an integral part of ongoing medicines development, with every patient potentially participating in real world evidence gathering (data privacy and consent notwithstanding). This can revolutionise every aspect of pharmaceutical medicine, providing greater assurance of data integrity and an ability to analyse it at every stage. With enhanced real time, real world benefit:risk evaluations, could we see this facilitating earlier but more targeted regulatory approvals and access, perhaps even with automated personalised labelling updates?

So, is this 'brave new world' a risk to the specialty of pharmaceutical medicine? Will pharmaceutical physicians still have a role?  
As many of us know, many company and payer decisions

are often based on financial measures. If this future possibility could cut the time and cost of development, and thus the financial risk, are we in a position to help it come about? Could we help build confidence in a more agile model of medicines development that can change the economics and improve the affordability of medicines based on more comprehensive real-world risk management? If we can, it will depend on our ability to leverage our experience and depth of patient understanding, as we develop new skills and capabilities that are relevant to a new world.

I hope it is a challenge we can rise to.

## ***FIND OUT MORE...***

*Starting on page 7 is an in-depth analysis of the definitions and sources of real world data and an update on the FPM working group.*



# WHAT IS REAL WORLD DATA?

## AN INTRODUCTION TO THE DEFINITIONS USED, SOURCES OF DATA AND POTENTIAL USES

FPM REAL WORLD DATA  
WORKING GROUP

DR MAYUR JOSHI  
(LEAD AUTHOR)

DR SEEMA PARIKH  
DR FRANCIS P CRAWLEY  
DR LODE DEWULF

### **Introduction**

The last two decades has seen an evolution in healthcare systems due to rising costs and capacity challenges, and, in tandem, the pharmaceutical industry has had to evolve with it. This evolving outlook has resulted in many new processes and pathways, including the increasing use of Health Technology Assessments (HTAs), and has impacted areas of drug pricing, access, and reimbursement, placing increasing pressure on life sciences companies. It is no longer the case that a product (drug, device etc.) will be used simply based on pivotal, registration studies. Wider data sources and consideration of the impact on the healthcare service are now key factors when assessing new technologies. This includes the overall financial impact of the product (not just acquisition costs), impact on the capacity of the healthcare service to provide the new technology (e.g. infrastructure for intrathecal medicines) and the funding mechanisms in place.

This need for broader types of information from a variety of sources beyond the randomised controlled trial (RCT), has led to a greater focus on Real-World Data (RWD) collection and the evidence that it generates (Real-World Evidence (RWE)).

The Faculty of Pharmaceutical Medicine (FPM) has several working groups focused on various innovative aspects of pharmaceutical medicine, including a RWD/RWE Working Group. Below we discuss the outputs of the working group, which looked into the various definitions of RWD/RWE and the wider implications.

### **Selected Definitions**

Currently, there is no single definition of what is meant by RWD or RWE. However, with increasing interest in real-world outcomes, several learned societies, regulatory bodies and other relevant organisations have commissioned their own reports with definitions, that the FPM RWD working group has summarised in Table 1 (overleaf), with comments. Some organisations have made an important distinction between RWD and RWE.

The definitions of RWD tend to sit outside of randomised-controlled trials, but this definition alone doesn't necessarily capture all potential data sources. The U.S. FDA definition, currently in medical device guidance, seems to be the most comprehensive in terms of naming multiple examples of data sources. However, strictly speaking, only

the ISPOR definition includes all RWD collection beyond the clinical setting (whether normal or routine).

In reality, the vast majority of a patient's time is spent living with disease away from clinical touch points and, whilst clinicians can collect information during consultations, this time spent away from the clinical environment represents an opportunity to learn more about the disease in the real world. Newer technologies are allowing this to occur in some cases with the use of wearable technology and connected devices, for example, but several of the definitions presented in Table 1 are still too narrow in this regard and focus on "normal clinical practice" or "routine care". This seems like a missed opportunity to include the patients themselves in the definitions. Thus, most common definitions of RWD are still at odds with the "patient centric" approach that both regulators and life sciences companies purport to be taking.

To further compound this apparent paradox, regulators are in fact looking at wider sources of data and types of information. For example, the FDA is already incorporating the "patient's voice" through disease specific Patient-Focused Drug Development (PFDD) meetings in order to expand understanding of living with the respective conditions. Similarly, the European Commission has recently stated its commitment to raise the level of interest in and use of Real World Data<sup>5</sup>. RWE collected directly from patients (through wearables, internet or testimonies) can help to guide research by answering questions related to burden of disease, burden of treatment and patient perceptions. This will not only help companies understand the patient experience of care better but also understand their experience of their disease thereby helping to make portfolio, research and development decisions. Clearly, therefore, this wider consideration 'beyond routine care' should also be incorporated in future definitions of RWD.

Furthermore, RWD does not only relate to medicines and can be related to any data collection outside of controlled environments like RCTs. This might include natural history studies, healthcare utilisation studies, patient reported outcomes, cost effectiveness studies, studies characterising costs associated with different treatment pathways as well as comparative effectiveness outcomes.

**The term "real-world data" can, therefore, potentially be applied to any data gathered outside of a controlled experimental setting.**

Table 1. Selected Definitions of RWD & RWE with FPM Working Group Comments

Organisation	RWD	RWE	Working Group Comments
<b>The Association of the British Pharmaceutical Industry – ABPI<sup>1</sup></b>	Data collected outside the controlled constraints of conventional RCTs to evaluate what is happening in normal clinical practice		A narrow definition as it contains “outside controlled environment” and limits scope to data collected within clinical practice. No reference to data collected directly from patient sources. Also raises the issue of what is “normal” clinical practice. Controlled pragmatic trials would be excluded in this definition.
<b>European Medicines Agency – EMA<sup>2</sup> (STAMP commission expert group)</b>	Observational data not collected under experimental conditions (randomised clinical trials), but data generated in routine care from information related to a patient’s treatment. It can come from patient registries, electronic health records, insurance data and web/social media.	Real world evidence is generated from such data sources according to a research plan. The research plan can be studies that are established to collect the data specifically for research purposes (primary data) or evidence coming from data collected for other purposes (secondary data)	Distinguishes between data and evidence by inclusion of the term research plan to generate evidence from the data.  Specifically mentions web/social media as potential data source.  Raises the question of what is “routine” care. Apparent contradiction between including web/social media while limiting to “routine care”.  Maintains “experimental and randomised” clinical trial in definition, therefore positioning of a pragmatic trial is unclear.
<b>International Society for Pharmacoeconomics and Outcomes Research – ISPOR<sup>3</sup></b>	Data used for decision making that are not collected in conventional RCTs		This is the broadest definition in that it does not limit RWD to the setting (e.g. routine medical care) or the source (e.g. patient).  The scope has a clear start (RCT) and open end, thus avoiding the issue of defining “normality” or “routine”, and includes also novel methods like pragmatic trials
<b>U.S. Food &amp; Drug Administration – FDA (medical devices draft guidance)<sup>4</sup></b>	Data collected from sources outside traditional clinical trials, may include large simple, pragmatic trials, observational /registry studies, database studies, case reports, healthcare claims, EHRs, public health investigation /surveillance, registries.  Typically derived from electronic systems used in healthcare delivery, medical devices, tracking the patient experience during care including home-use settings.	Evidence derived from aggregation and analysis of RWD elements	Clear distinction (like EMA) between RWD and RWE, specifying terminology “aggregation and analysis”.  Patient sources (in terms of medical devices) included in definition, but Patient and care giver surveys are not mentioned as sources neither is social media specifically mentioned and neither are claims databases  Pragmatic trials specifically listed as included in scope.



## RWD vs RWE

The terms Real-World Data and Real-World Evidence are often used interchangeably but, in reality, they are different concepts. RWD is the actual raw data, retrieved from a myriad of sources (registries, electronic health records, patient reported outcomes, wearables, testimonies, surveys etc.), that may be unstructured or structured. RWE is derived from the aggregation and analysis of this data. It is the product of analysed RWD and results in meaningful insights into the disease area. This can range from individual studies published in peer-reviewed journals to the use of analytics engines to give real-time insights using data sets.

Both EMA and FDA make a clear distinction between “data” and “evidence”, the latter specifically calling out the aggregation and analysis of data elements to develop evidence, and the EMA focusing on the need for a research plan to be in place for such scientific approach.

This distinction between RWD and RWE is indeed very relevant. Whereas historically (in RCT) the scientific rigour was applied to source (physician), nature (medical) and analysis (stats) of data, what is happening with RWD is that the first two (source and nature) are being broadened. The third, however, remains what turns data into evidence. The regulatory authorities have been quite clear on this point, including in a recent public FDA workshop: what makes RWD into RWE (and thus the only thing they will consider) is the data and its analyses meeting scientific rigour (especially the criteria of representativeness and significance), for which you need a plan before you start analysing (even collecting). Pharmaceutical physicians have an important role to play in raising the understanding of this difference.

The common theme of RWD and RWE is one of data collection outside of artificial environments. A randomised controlled clinical trial usually has strict inclusion/exclusion criteria; patients are also randomised and the study population is, therefore, not necessarily representative of the target patient population. In addition, the monitoring is highly controlled and not necessarily representative of clinical practice. The aim of RCTs is to minimise bias and confounding in order to answer a specific question; in the case of the pharmaceutical industry this is usually to provide proof of efficacy of a medicine against placebo or standard of care, establishing causality between wanted and unwanted effects of a medicine. In contrast, real-world data collection is focused on the use of the medicine in clinical practice where the population is much more heterogenous compared to RCTs, may have many co-morbidities and may receive concomitant medication.

As such, RWE evidence can be (and is increasingly being) used beyond the context of drug approval, pricing and reimbursement. RWE can, indeed, also help to make better decisions earlier in the life cycle, including as far as the selection of research areas. RWE may thus inform direct clinical decision making on the choice of medicines (e.g. comparative effectiveness or natural history studies) or decisions related to the economic impact of technologies

(health economic outcomes research) or improving patients’ experience of care (e.g. through social listening in a hospital setting), benefit-risk assessments or setting R&D priorities.

**This distinction between RWD and RWE highlights the importance of the (planned) purpose of the data collection, of the scientific rigor used to develop meaningful insights to inform decision making. Data without purpose has no utility; data without method is not evidence. The same RWD might be used to produce various types of RWE and this will depend on the specific question asked and the analytical methods used.**

## RWE Complements RCT Evidence

One of the key objectives of RWE (for the pharmaceutical industry) is to understand outcomes in routine clinical practice and in this regard, RWE complements the efficacy and safety data generated by RCTs. RWE doesn’t fit into the traditional hierarchy of evidence (Fig 1), where RCTs are still the gold standard in determining efficacy, but can provide valuable information for populations not assessed in the trial environment, for example. RCTs test specific questions in a controlled, experimental environment with carefully developed protocols and, therefore, do not represent actual use of the medicine or device in clinical practice. The data they provide is essential in terms of proving causality, whilst RWE can provide information on overall effectiveness in wider patient groups. Outside of the highly prescriptive environments of clinical trials, confounders such as adherence and co-morbidities are not controlled for, giving us a better picture of how the drug performs in the target population.

The U.S. FDA and the EMA have both formally acknowledged the need for the increased use of RWE in supporting medicines whilst, in Asia, Japan has already begun their “Rational Medicine” initiative to make the Japanese health care system more patient-centric and evidence-based<sup>8</sup>. Regulators around the world are incorporating RWE into their decision-making as evidenced by the FDA’s aim to produce formal guidance on the use of RWE by 2021 and the EMA’s adaptive pathways approach<sup>9,10</sup>. Lifesciences companies naturally need to ensure they are evolving and adapting to this increasing demand for RWE.



Figure 1. Hierarchy of Evidence<sup>6,7</sup>

The use of RWE has, to date, largely been restricted to the period just before launch and through the post-marketing phase, to better understand patient populations, drug safety and for comparative effectiveness studies against existing products. These studies may also be incorporated into health economic modelling to inform pricing, reimbursement decisions based on cost effectiveness and the wider impact on the healthcare system by evaluating resource allocation. As the use of RWE becomes more well established, with regulators making licensing decisions, more companies are starting to incorporate it into earlier stages of clinical development programmes. Some companies are also leveraging RWE to guide their research efforts, based on a better understanding of more dimensions of the burden of disease, which can help to identify new patient relevant targets. However, whilst the potential to improve development relevance and thus impact is clearly an attractive proposition, many companies are still waiting for more clear guidance and standards from healthcare decision makers.

### **Conclusions**

There is increasing recognition within the life sciences sector and the healthcare industry of the need for a variety of evidence beyond RCTs when it comes to developing and evaluating therapy areas (including medicines). This is reflected in the increasing volume of real-world studies being published, the increased recognition by regulators of the value of RWE and the

increased use of RWE to convey messages around (cost) effectiveness and safety. However, there are many hurdles to overcome before real-world studies are universally accepted. Some of these hurdles will be overcome with the publication of guidance and standardised methodology, whilst other hurdles will be overcome with greater transparency from industry and improved education of stakeholders.

**As discussed above, three themes emerge from this review:**

- 1) 'Data collected outside of RCTs' seems to be the common theme in current definitions of RWD/ RWE, but the differences beyond that introduce uncertainty or limit the scope.**
- 2) The distinction between RWD and RWE is important and relevant to decision making and starts with a plan. RWE can drive decisions throughout healthcare and the medicine lifecycle.**
- 3) Real-world studies complement and do not replace RCTs.**

### **Interactive question...**

**The FPM Real World Data working group is planning to organise a workshop on advanced topics in real world data in December - which specific aspects of RWD would you like to see covered?**

**Disclaimer: By completing the above form you consent to your comments being read by the real world data working group. Comments will not be printed or shared without your express permission. Your name and email will not be shared.**



## References

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# REPORT FROM PHARMACOGENETICS AND STRATIFIED MEDICINE NETWORK – 5TH ANNUAL OPEN MEETING

The only critical thing one can say about this meeting and this network is its cumbersome name, which you have to look up every time you want to talk about it. Apart from that, this is an outstanding success story for the NHS: a many-faceted network of scientists and medics interested in the burgeoning field of pharmacogenetics and personalised, or stratified, medicine. The Network was set up in 2012 by Professor Sir Munir Pirmohamed, a distinguished clinical pharmacologist (where have they all gone?) who is David Weatherall Chair in Medicine at Liverpool University. He has done a terrific job of bringing together a disparate group of stakeholders (excuse the well-worn phrase), across academia, industry and the NHS firmament. There are 700 members and growing.

Until you attend one of these meetings you may have no idea of the importance of the genetic profile for drug efficacy and safety. For example, in one of his two talks, Professor Pirmohamed described the influence of two of the 'pharmacogenes' - CYP2C9 and VKORC1 - on response to warfarin: by tailoring the dose based on the presence or absence of these two genes, using a clinic-based testing kit, the percentage of patients within the optimal INR (international normalized ratio, evaluates the pathway of coagulation) range over a period rose from 60% to 67% - in a trial setting. Similarly, the risk for Type B (non-target) adverse drug reactions, which are the severe ones, are determined by HLA type (cell-surface antigens that regulate the immune system): 85% of us have one or other HLA risk allele which predicts an adverse reaction to one of the common drugs used. Knowledge of the HLA phenotype can be used to avoid these reactions (by avoiding the relevant drugs) especially in elderly patients on multiple drugs. Professor Pirmohamed showcased a dashboard of the future, which could be made available to GPs, in which the clinician clicks on a drug they want to prescribe (like warfarin, or captopril), and the system tells them which gene tests to order. In two weeks, the results will be back, if the vision for gene testing in the NHS is realised. If you have seen Decision Support technology at work in your GP's surgery, for example for assessment of cardiovascular risk (in 30 seconds), you will realise that this is a feasible proposition.



*Watch Professor Pirmohamed introduce the NHS England Personalised Medicine Strategy*

Other speakers spoke about the stratification of three diseases by means of genomic testing – asthma (Ratko Djukanovic from Southampton), psoriasis (Prof Chris Griffiths, Manchester), and Primary Biliary Cholangitis (David Jones, Newcastle). In each case, combinations of proteome and whole gene sequencing – many years of painstaking work – has led to an understanding of the subtypes of these diseases, and their accompanying differential responses to different therapeutic interventions. This is leading to new subtype classifications of these and other diseases, which will find their way into the textbooks in due course.

Tom Lillie, head of European Clinical Research at Merck, gave an excellent talk on PD-L1 inhibitors, and described the “tsunami of data” which is about to descend on regulators from the myriad trials being conducted in multiple indications for several of these drugs: so much so that trial activity now needs to be depicted on a graph. Never before have the regulators been asked to assimilate so much new data at once, and it will prove challenging. Some members of the audience suggested that the sheer quantity of trials is excessive and duplicative but Dr Lillie pointed out that these patients are all seeing potential benefit from the trials; though he did acknowledge the enormous duplication. He presented data linking likelihood of response to the mutational load of a patient's tumour, and to the gene expression profile of that patient – each independently predictive of response.

**DR GILLIES O'BRYAN-TEAR**  
CHAIR, POLICY AND COMMUNICATIONS GROUP, FPM



This is a much more effective way to predict response to PDL-1 inhibitors than conventional immunohistochemistry, which is subject to observer variability and to variability between the four assays currently available in the market. The latter is a big issue, if you imagine being the patient, who might be told "well on this test you are positive, but on that test, you are negative, so let's give you Keytruda anyway". Not exactly confidence-inspiring for the patient. There were presentations from the National Institute of Health Research Clinical Research Network (CRN) (Michael Beresford), describing the contributions which the CRN can make to the design and conduct of genomics trials in the NHS; Innovate UK (Karen Spink), describing the funding available from this government backed source for technology development and start-up companies in the field of Precision Medicine, amongst other fields; and Professor Pirmohamed (standing in for Sue Hill, CSO for NHS England) describing the rollout of a sophisticated gene testing service in the NHS. The focus of this initiative is initially on rare diseases and cancer, but will be expanded to include drug safety issues.

Stuart Doyle gave a moving account of what it was like to suffer life-threatening Stevens-Johnson syndrome (which was idiopathic) in his 20's: he lost most of his sight from cicatrisation of the eyelids and scarring of the corneas; he lost his nails, and nearly his life; and he lost his wife and child to Australia. He has written a book about his experiences, and he ended by making a gracious tribute to the many scientists and medics who are working hard every day to understand genetic risk, and how we can harness this knowledge to prevent the kind of things that happened to him.

This was a fascinating scientific day with a large number of industry, academic and healthcare attendees: the Faculty of Pharmaceutical Medicine has a long-standing affiliation with the Network and has attended for the last three years: I can thoroughly recommend it for next year, when it will be held on 20th March 2019 in London.



Professor John Savill, outgoing Chief Executive of the Medical Research Council (MRC), gave an overview of the research and expertise which has been the subject of £75m of MRC investment: 17 Molecular Diagnostics centres, with 37 academic and 57 commercial partners; big numbers for a big field of endeavour.

**FIND OUT MORE...**

To watch additional presentations and find out more about the Pharmacogenetics and Stratified Medicine Network click on the arrow...



# MY LIFE IN PHARMACEUTICAL MEDICINE

Where do I start? 1989.

Having worked as a chest physician and in other areas of medicine for many years, I was looking for a new challenge. I enjoyed what I was doing but, frankly, I was a bit bored! I knew little about the pharmaceutical industry but became intrigued. Instead of knowing you were doing bronchoscopies every Friday, and clinics every Tuesday and Thursday, I discovered that every day had the potential to be different. After a lot of soul searching, I launched into a new career. Some thought I was mad, my parents were shocked, but this was new, exciting, and unknown.

For the most part, I was driven by what has always been my motivation – patients. No, I wouldn't be treating individuals but rather populations. The concept of helping thousands or millions was attractive. My industry career has been largely unplanned; opportunities and challenges appeared, stretching my thinking and developing me as an individual, working as part of hugely inspiring teams. I worked with amazing people, far more knowledgeable and talented than I ever have been.

During my career, I have had some significant challenges that live long in my memory. In one example, issues with antidepressants where the media attacked the industry (and GSK in particular) when I was running the Clinical Psychiatry division. The conventional approach was to weather the storm, keep your head down and wait for it to blow over. I didn't agree and persuaded the company, by going to the very top, to listen and give our perspective externally. I wanted to ensure patients had the opportunity to be heard, but also to benefit from an important product. I met with patient groups, some who were suing us, some who just wanted to be heard. I visited them, including in their homes, and listened and gave a 'human' industry perspective which they valued. I had multiple difficult experiences bringing an industry and patient view on news bulletins, chat shows (e.g. Richard and Judy) and several interviews for Panorama. I discovered (especially on Panorama) that the producers often weren't interested in facts or benefit, only a story where industry and I were the bad guys. The personal attacks in the media, on social media and by individuals, continued for years and still, occasionally, resurface.

Would I engage with patients in this way again? I think so.

Better prepared for sure, and realising that you have to do this in addition to the day job. But fundamentally, because standing up for the patients we serve, the benefits we bring, and the value of pharmaceutical medicine in bringing new medicines to market and keeping patients safe, is so important to me. Being prepared to put our point of view forward is important; we need more people to do it.

After many other roles, I moved into the not-for-profit sector as a Chief Executive of the European Brain Council, initially for two months which became three years, working with patient groups, academia, industry and the European Commission. I then moved to Kinapse, a management consultancy and operational services provider for three years and now I am back in mainstream pharma at Norgine, bringing many products to patients in many disease areas.

I was once told to surround myself with talent and bathe in their reflected glory. I am fortunate that I have done this and worked with wonderful people, hugely talented and patient focused from administrators to chief executives. Would I change anything? Would I do it all again? 'Yes' to both, but I prefer to learn, adapt and develop. As pharmaceutical physicians we benefit millions of patients around the world. Always have them in mind; do the right thing at the right time, in the right way; challenge conventional thinking; be creative; but enjoy yourself and create a fun working environment for all. Together we can achieve so much and we should all be proud of what we do. Every day we can make a difference to the patients we serve. The future rests with you.



# DR ALASTAIR BENBOW

CHIEF DEVELOPMENT AND MEDICAL OFFICER  
NORGINE



<b>My Career in Pharmaceutical Medicine 1989 - present</b>		
Fisons	Physician Research and Development	1989 - 1992
	Clinical Research Manager and Medical Advisor	1992 – 1994
Genentech	Medical Director UK	1994 – 1995
Royal Brompton Hospital	Clinical Fellow CF Unit	1994 - 1995
Loxex Synthelabo	Medical and Regulatory Director	1996 – 1997
SmithKline Beecham	Medical Director and VP Clinical Research and Development and Medical Affairs	1997 – 2000
GlaxoSmithKline	VP European External Relations, Government Affairs and Public Policy	2001 – 2002
	VP and Head of European Clinical Psychiatry	2002 – 2004
	VP and European Chief Medical Officer	2004 – 2009
	SVP Global Clinical Safety and Pharmacovigilance and EUQPPV	2008 – 2009
	SVP Policy Development	2010
European Brain Council	Chief Executive	2010 – 2012
Kinapse	Chief Medical Officer and Head of Operational Services	2013 – 2016
Norgine	Chief Development and Medical Officer	2016 - present
<b>Other</b>		
ABPI Medical Committee		1997 - 2000
ABPI Code of Practice Appeals Board		1998 - 2002
Chair of Ethics and Practice Faculty of Pharmaceutical Medicine		2017 – present



# FPM NEWS

## PROFESSOR TIM HIGENBOTTAM TO BE THE NEXT PRESIDENT OF THE FPM

The Faculty of Pharmaceutical Medicine is pleased to announce that Professor Tim Higenbottam FFPM has been elected as its next President. Professor Higenbottam, currently Vice President, will take up office on 1st November 2018.

Professor Higenbottam commented "I am delighted and honoured to have this opportunity to be the next President of the Faculty. As a pharmaceutical physician with over 30 yrs experience, first in the NHS, in academia, in big pharma, biotech and consulting, I hope to build on Professor Boyd's achievements by sustaining the outward looking Faculty and voice of authority for pharmaceutical medicine professionals.

Pharmaceutical Medicine is a specialty that dedicates itself to ensuring that the physicians involved meet incredibly high standards. Pharmaceutical physicians have a critical role in study design, data generation, accurate reporting,



ultimately achieve approval, and then oversee products. The success of the PMST and value of the CCT has brought more members to the Faculty especially from overseas, whilst appraisals/ revalidation has encouraged membership of our independent consultants. I will be looking for the growth of the membership through focused support for all classes of membership. I hope that I can count on members' support as Pharmaceutical Medicine is entering a phase of critical importance, both for medicines innovation and UK economics (UK Health Sciences Strategy)."

## NEW FPM STAFF

**Will Strange**  
*Marketing and Development Manager*

Will has joined the FPM in the new role of Marketing and Development Manager, and brings his experience of working at membership organisations and learned societies within the STEM sector. Outside of the FPM Will is in the final stages of a marketing diploma, as well as being a professional wedding and event photographer.



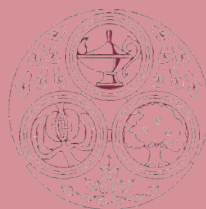
Marianne Whitelam

### *Examinations and Standards Manager*

The newest member of staff to join the FPM is Marianne, who has taken over the role of Examinations and Standards Manager. Originally from Sweden, Marianne has been in the UK since 2006 and has spent several years working in both Examinations and Assessment at the Royal College of Paediatrics and Child Health. She most recently held the role of Senior Examinations Coordinator at the Royal College of Pathologists and is now looking forward to getting to know more about the field of Pharmaceutical Medicine and working alongside faculty staff and members.







## GMC REVIEW OF PHARMACEUTICAL MEDICINE VIRTUAL DEANERY - INITIAL FEEDBACK

### MR KONRAD OBIORA SPECIALTY TRAINING MANAGER, FPM

The GMC recently completed a review of the Pharmaceutical Medicine Specialty Training (PMST) programme and the Pharmaceutical Medicine Virtual Deanery as part of its responsibility to quality assure approved UK specialty training programmes.

A small GMC visit team met the Deanery staff and groups of trainees, Educational Supervisors and Specialty Advisers between 5 February 2018 and 13 April 2018. The meetings were hosted by the FPM, and Local Education Providers (Boehringer Ingelheim, GlaxoSmithKline and Sanofi), and were an opportunity for the visit team to speak to people involved in the PMST programme, and to check that the Deanery is meeting the standards set out in the GMC's Promoting excellence: standards for medical education and training.

## General Medical Council

The visit team is currently writing its report, which will be published on the GMC website in due course. The visit team gave the Deanery initial feedback at the end of the review which overall was positive. They remarked that they found the trainees whom they met to be highly motivated and dedicated to their professional development, and demonstrated their enthusiasm and genuine support for pharmaceutical medicine. The visit team did identify areas of improvement that the Deanery should consider, such as providing guidance on recognising and supporting trainees in difficulty and addressing the current perception of the ARCP process. The FPM's Deanery Executive Group and the JRCPTB's Specialty Advisory Committee on Pharmaceutical Medicine will consider the report after it has been published.

The Deanery would like to thank the 39 trainees, Educational Supervisors and Specialty Advisers - some of whom braved the heavy snow storms during February and March - for taking time out of their busy schedules to meet the GMC visit team. We would also like to express our gratitude to Boehringer Ingelheim, GlaxoSmithKline and Sanofi for hosting the meetings.

### PROFESSOR GEETA MENON APPOINTED AS POSTGRADUATE DEAN FOR THE PHARMACEUTICAL MEDICINE VIRTUAL DEANERY



The FPM is pleased to welcome Professor Geeta Menon who takes over from Dr Andrew Frankel as the new Postgraduate Dean for the Pharmaceutical Medicine Virtual Deanery. Geeta was also appointed as the Postgraduate Dean for Health Education South

London following Andrew's retirement from this position. In addition to her duties as postgraduate dean, Geeta is a Consultant Ophthalmic Surgeon at Frimley Health NHS Foundation Trust.

We would like to thank Andrew for supporting the specialty as our postgraduate dean, and we look forward to working with Geeta.

# REVALIDATION - FIVE YEARS OLD

DR SUSAN BEWS  
RESPONSIBLE OFFICER  
FPM



Back in December 2012, the end of the first five-year revalidation cycle seemed a long way off, but we have now just completed that first full cycle. I looked back at the July 2012 Faculty Newsletter and in my opening statement I said that 'I came across some notes from late 2002 headed 'Revalidation'. They related to what would be needed for the 'imminent introduction' of revalidation and mainly concerned CPD... As with anything new, there will be challenges as revalidation beds in. There will inevitably be aspects to it that we think are too onerous, irrelevant or time consuming. However, I do believe that the GMC have introduced a reasonably pragmatic, workable system, which will give patients and the public confidence that the doctors who are responsible for their health and welfare are up to date and fit to practice in the area in which they work'. The gestation was lengthy, but at the end of this first cycle I do think we have seen the birth and early maturing of a very functional, relatively pragmatic, system. In fact, I am often heartened by the comprehensiveness and flexibility of the GMC revalidation process and its capability to accommodate over 200,000 doctors carrying out a very varied range of roles.

The numbers connected to the Faculty have risen from just about 500 to around 600 in those five years (with a substantial yearly turn-over of up to 100 doctors leaving and another 100 (re)joining in a year). This makes us one of the larger designated bodies in the country - out of the 776 current designated bodies we are ranked 87 by the number of doctors with a connection to us. I have made over 800 revalidation recommendations to the GMC. As a designated body that does not employ any of the doctors revalidating through us, we face specific issues that are not widely replicated across the profession. Some of the implications were not anticipated when revalidation was introduced, but with hard work from the revalidation staff team, appraisers, and of course appraisees, we have improved the quality and personal benefit of appraisals. As all revalidating doctors know well, it takes a significant amount of time to prepare a satisfactory portfolio that meets GMC requirements. Inevitably some consider that the requirements are burdensome, but we need to look at the requirements from a patient perspective - what evidence would patients and the public need to be assured that a doctor is up to date and fit to practice, and continually seeking to improve that practice. I find it very reassuring that any doctor I or my family and friends may see is subject to the requirements of revalidation and needs to provide, annually, sound evidence across the various types of evidence and that the appraisal discussion focuses on the tenets of *Good Medical Practice*.

Our processes and policies have changed over the years to offer better support, whilst ensuring compliance with the GMC and NHS England as revalidation bedded in. The overall conclusion from the report of the 2016 external quality assurance review was 'exceptionally positive', commenting that it was evident that the Faculty achieved a high level of consistent practice demonstrated by appraisal portfolios containing good

reflection, meeting *Good Medical Practice* requirements and a culture of continuous improvement with good to outstanding quality examples within the appraisal documentation. We are not complacent though and continue to review our processes regularly to improve as well as keep up to date with changing requirements and shifts of emphasis. We welcome feedback and suggestions as to how we can all more effectively meet our obligations and contain the work that must be done to achieve this. As examples, from the valuable, recently issued update to the GMC *Guidance on supporting information for appraisal and revalidation* emphasises quality, not quantity of supporting information, and inadequate reflection is now a documented reason for unsatisfactory engagement, alongside missed appraisals. If you are not already aware, the GMC has also updated the whole of its website and it is certainly easier to navigate.

If you are revalidating through the Faculty please do take advantage of the support offered to you and if you face challenging personal circumstances let us know. The sooner we know, the sooner we can assist and the system is here to advise and support you through challenging times. So many issues can be resolved with an email or phone call and it is best to tackle them early on.

On a national level, between 3 December 2012 and 31 March 2018, 192,310 doctors have been revalidated by the GMC, 46,493 doctors received a deferral and there were 626 recommendations of non-engagement for a total of 239,429 recommendations. This has required a huge amount of work at many levels across the medical profession and administrative staff and we are just starting to see the first cycle reviews released by the GMC. The focus for the next five years is to be around continuing to embed revalidation and ensuring value-added annual appraisals by improving the quality of appraisals but not by increasing the amount of work for doctors.

Finally, I would like to thank the Faculty Chief Executive, our Presidents and the Board for their support of revalidation these past five years. Becoming a designated body was a major step for the Faculty to take, adding new statutory and regulatory functions related to a doctor's licence to practise to a membership organisation. It has inevitably changed the relationship of one part of the organisation with many of its members but I believe that in doing so it has enhanced the Faculty as a whole, both internally and externally. Setting up the Designated Body posed challenges, but the personal and institutional commitment to, and support for, revalidation has ensured that pharmaceutical physicians can have both a vibrant membership organisation and in parallel a robust designated body for those who require it. We do not know the challenges of the next five-year cycle, but based on the last five years, I am confident they will be met not just by the Faculty as an organisation, but by the individual members who are a part of it as appraisers and appraisees.

# Events at the Faculty



We have an exciting calendar of upcoming events at our Angel Gate headquarters. View our website for details.



## **Culture: Skills for Global Working**

**Date: 27th September**

**FPM members rate: £350**

**Non FPM members rate: £400**

A one-day business skills workshop developed for the Faculty by the Learnlight Group Ltd. Learners will improve their understanding of key drivers of organisational, sector and national culture and develop practical strategies for working globally and communicating effectively in diverse teams. The workshop size will be limited to twelve people with some digital self-study activities for preparation and consolidation offered before and after the workshop.

**BOOK**

## **Business Skills: Gravitas**

**Date: 22nd November**

**Members: £350**

**Non-members: £400**

We have collaborated with Antoinette Dale Henderson of The Gravitas Programme to develop a tailored one-day business skills courses with sector-specific learning outcomes that will add great value to the professional development of pharmaceutical physicians, whether employed in industry or working independently. The first session has sold out so we have negotiated a repeat session for later in the year. Book early to avoid disappointment.

**BOOK**

Royal College  
of Physicians

## Innovation in Medicine 2018

RCP Annual Conference ExCel London, 25th - 26th June 2018

We will be showcasing the work of the Faculty as well as championing the specialty of pharmaceutical medicine to over 1000 delegates at the upcoming **Innovation in Medicine 2018** RCP annual conference, 25th - 26th June.

We will have an exhibition booth in the Charity Zone, near the main theatre, so please do take the opportunity to meet our staff and your member peers if you are in attendance.

FPM members are eligible for the RCP members' registration fees - when registering, click 'yes' to 'Are you an RCP member?', and then enter 'FPM' as your membership number.

You can find out more about the event at <http://rcp-medicine-conference.com>

### **'The future of medicines: what treatments will we be using in 30 years' time?**

**Monday 25th June, 3.00 - 4.30pm**

FPM President, Professor Alan Boyd is chairing this must-see concurrent session at the conference. Don't miss out on this opportunity to hear presentations from Dr Freda Lewis-Hall, Mr Andrew Thompson and Dr David Chiswell.



# ENGAGING WITH THE PHARMACEUTICAL INDUSTRY AND WHAT THIS MEANS FOR CLINICIANS

Clinical healthcare professionals (HCPs) often encounter employees of all kinds who are working in the pharmaceutical industry. However, they are sometimes unsure about how to interact with industry, and what is and isn't acceptable in such relationships. The Association of the British Pharmaceutical Industry (ABPI) Code of Practice provides clear guidance to those within the industry, but can sometimes be confusing and difficult to navigate for HCPs, who may feel unable or unwilling to engage.

A working group of the FPM is currently working on a resource for clinical doctors and all healthcare professionals to inform and support this relationship. It aims to outline the responsibilities incumbent on HCPs to maintain an appropriate relationship with industry. Herein we provide an update on the progress of the working group.

At the core of the relationship between clinicians and the pharmaceutical industry is the scientific exchange and sharing of knowledge about diseases and therapies to improve patient outcomes. This collaboration is critical in ensuring that patients' medical needs, potential therapeutic solutions and the everyday application of treatments in clinical practice are effectively and appropriately assessed and communicated. It is also vital in establishing and managing the benefit/risk balance of medicines.

These relationships take many forms and the guide attempts to summarise the main types of exchange. It also sets out the appropriate outputs, acceptable behaviours and relevant best practices. It aims to advise healthcare professionals (HCPs), such as doctors, nurses, and pharmacists, in their most frequent interactions with the pharmaceutical industry, encouraging a deeper understanding of common standards and requirements, and clarifying the responsibilities of the different parties.

HCPs' codes of conduct also give guidance on expected and required behaviours. For instance, Good Medical Practice from the GMC sets out clear advice for registered doctors: 'You must not allow any interests you have to affect the way you prescribe for, treat, refer or commission services for patients'. The FPM guide builds

upon established industry and regulatory guides and codes, as well as guidance for clinical doctors and other healthcare professionals from the General Medical Council (GMC) and other international bodies.



The FPM's guide will be divided into three sections, each complemented by common examples and frequently asked questions (FAQs). It focusses on interactions with the pharmaceutical industry, but also takes account and explains some of the differences across sectors, including biologicals, devices and diagnostics.



**DR KAREN MULLEN**  
CHAIR, 'CODE FOR CLINICIANS' WORKING GROUP,  
FPM



**DR BEN COTTAM**  
POLICY AND COMMUNICATIONS MANAGER, FPM

### **Section 1 – Ways to interact**

Clinicians and other medical professionals can offer the industry invaluable insights into areas of unmet medical need, disease background, potential therapeutic solutions and the everyday application of treatments in the clinic. In turn, the industry can provide HCPs with the opportunity to provide their expertise to pioneering R&D programmes, develop the therapeutic landscape through clinical research programs, conduct scientific discussions and participate in medical education.

This first section focuses on common interactions between HCPs and industry representatives: including:

- distinctions between promotional interactions and non-promotional meetings and activities
- participation on advisory boards
- medical education programmes
- the concept of fair balance
- MEGS
- joint working
- side effect and adverse drug reaction reporting

It also explains the different roles and remits of industry departments and personnel.

### **Section 2 – Conflicts of interest and transfers of value**

This section outlines how different conflicts of interest might arise and how HCPs can deal with them. It starts by stating the NHS definition of a conflict of interest as being:

*'A set of circumstances by which an observer would consider that a HCP's ability to apply judgement or act, in the context of delivering, commissioning, or assuring taxpayer funded health and care services is, or could be, impaired or influenced by another interest they hold.'*

The FPM guide goes on to encourage all HCPs faced with a conflict or potential conflict of interest to be transparent and declare the conflict formally. It also discusses disclosure of transfer of value and outlines the rules around hospitality.

### **Section 3 – Agreements, permissions and confidentiality**

The final section of the guide details the various agreements and permissions that HCPs may be required to agree and adhere to when working with industry. The guide stresses the importance of confidentiality, both in terms of patient information (outlining the special circumstances under which patient information can and should be disclosed) and commercially sensitive information. The guide encourages HCPs to consider whether they are the most appropriate person to undertake the work, whether they are being paid fair market value and whether the contract accurately reflects the service they are providing.

The working group is currently seeking the advice on the draft guidance from external stakeholders including the ABPI and the Royal College of Physicians. We are aiming to publish the guidance in the summer 2018.

#### **Interactive question...**

*What do you think is the most common misconception amongst HCPs about working with industry?*

Disclaimer: By completing the above form you consent to your comments being read by the 'code for clinicians' working group. Comments will not be printed or shared without your express permission. Your name and email will not be shared.

# FPM CONVERSATION: “ETHICS IN CLINICAL TRIALS” AN EVENING WITH PROFESSOR JOHN HARRIS

On 30th January 2018 Professor John Harris joined us at the FPM to raise an excellent discussion and spark debate around the 'Ethics of Clinical Trials'. As a kindred spirit to Plato waxing philosophically, Prof Harris remarked that whilst Plato may have on occasion used visual aids, in the form of shadows on the walls of a cave to highlight his stories, he himself abstained from the use of slide presentations. We've summarised some of the key threads from our robust and engaging conversation, some of which we hope to pick up on during the FPM Education Day on the 12th June.

## ***The Freedom of Science***

During the inaugural dinner at the White House, one of President Obama's colleagues asked if they were going to redact certain content from a presentation. The chief general of the White House responded: "Anything digitalised can be hacked". Indeed, in a dawning era of big data and transparency, true privacy has become increasingly elusive.

When it comes to patient autonomy, surely there is a moral and prudential argument to pursue scientific research, and an obligation as members of society to partake. If indeed we measure our success and wealth by the health and wellness of the most vulnerable, how do we set about ensuring we have solutions that serve to protect their health and wellbeing?

Paediatric research has remained one of the biggest conundrums for the scientific community, with paediatric oncology showing one of the lowest clinical trial uptake whilst having a high unmet therapeutic need. What are the obligations and ethical considerations around children and what is their role in scientific research?

## ***Benefit to Society vs. Individuals***

Assuming that people do want to participate in research, should we all have a moral obligation to help others? If immunisation schemes had not taken place would we have been able to eradicate small pox? Should we all be responsible citizens and 'reflective moral agents'? Ultimately, research benefits the greater good.

The World Medical Association *Declaration of Helsinki* states that 'While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects'. However, Professor Harris was strongly opposed to this sentiment. What if medical research was mandatory like jury service and what happens if you do not take part – should you be penalised or not benefit from the treatments later made available?

Being or becoming a research participant doesn't augment human/fundamental rights, but it is morally important. Doctors also swear an oath to 'do no harm' but how is this possible if they do not know the outcome or what repercussions may arise from patients' involvement? How do we consider public safety standards versus protecting an individual's right to choice?





**DR SANGEETA MITTAL**  
 SENIOR MEDICAL AFFAIRS AND COMPLIANCE DIRECTOR  
 INTEGRATED MEDHEALTH COMMUNICATION



**DR KAM NANUWA**  
 MEDICAL DIRECTOR  
 IDACO CONSULTING LTD.

***The UK clinical research environment – competing on an international platform***

The sustainability of our current approach needs rethinking, as do the economic considerations around research and development programmes, especially considering the global platform on which we now compete. How do we secure funding streams to sustain the UK clinical and academic research environment?

The conversation participants discussed the pros and cons of real world studies versus extensive phase III clinical trials. Is the answer for pharmaceutical companies to work together for the greater good or should we move the ethical obligations around clinical trials to pharmaceutical companies e.g. compassionate use programmes? As such, should clinicians and patients be obliged to collect registry data, inclusive of patients receiving novel therapies through such programmes? Should they work collaboratively with pharma companies, to ensure publication of the data, and that it is included in submissions to the regulatory and commissioning bodies?

Prof Harris suggested an adapted Helsinki Declaration - 'biomedical research with humans cannot be neglected and is permissible and therefore mandatory'. This sparked a final debate on how high standards would be established and maintained and whether participation in clinical research, be it funded through academia or pharma, should be made a national opt out, rather than opt in, scheme.



***FIND OUT MORE...***

*Interested in medical ethics?*

***Register now for the FPM Education Day  
 Applying ethical values and good practice in pharmaceutical medicine on the 12th June...***



# GDPR: A TOPICAL SUBJECT - PRIVACY AND SECURITY OF CLINICAL DATA

The EU General Data Protection Regulation (GDPR) published in 2016 is effective from 25<sup>th</sup> of May 2018 – there is no transition phase. As pharmaceutical physicians, we all should be aware of the changes that will occur to the manner in which we can collect, process and disclose patients' data. If we are not all aware then perhaps this short review will alert us (useful URLs are provided for reference).

## **Background**

This EU GDPR replaces the existing Data Protection Directive (DPD). It extends the rights of individuals over their personal data and places significant new security requirements on the storage of data. **Unlike the DPD, a regulation is a binding piece of legislation that is enforceable by all member states.** Failure to comply with the regulation will leave a company, organisation or individual open to fines that can rise to \$20 million or 4% of total global turnover, whichever is the larger. Member states would apply the penalty through an independent public authority established, pursuant to Article 51 of the regulation. The UK will probably use the existing Information Commissioner's Office (ICO). The present commissioner is Ms Elizabeth Denham.

Whatever the results of the Brexit negotiations, GDPR will apply to businesses in the UK. The UK government's new data protection legislation (The Data Protection Act 2018), will implement all the main areas of the regulation. However, there is some flexibility on how individual countries implement GDPR. The UK will include extra protection for journalists, scientific and historical researchers, anti-doping agencies who handle people's personal information, and children's data.

GDPR is the most recent regulation to protect privacy and to provide security of data but has its origin in the European Convention of Human Rights (ECHR) of 1953. Article 8 of the ECHR reads:

*1) Everyone has the right to respect for his private and family life, his home and his correspondence*

*2) There shall be no interference by a public authority with the exercise of this right except such as is in accordance with the law and is necessary in a democratic society in the interests of national security, public safety or the economic well-being of the country, for the prevention of disorder or crime for the protection of the rights and freedoms of others*

Globally, most countries have developed such regulations but in recent times, it has become necessary to expand their remit to ensure compliance. This reflects the concern of society about

the abuses of the use of data and the insecurity of its storage. As part of the "Digital Revolution", we are experiencing huge expansion of Internet use, particularly with mobile devices, where there were only there were 92 million mobile subscribers in 1995, now rising to 6.91 billion in 2016.

It is important to remind ourselves of the serious nature of the recent breaches in data security and abuse of private data, for example:

- Carphone Warehouse who were fined £400,000 by the Information Commissioners Office for a number of inadequacies found during an investigation of the hacking of 3 million customers' data in 2015
- Uber failed to report and paid an undisclosed ransom after 57 million people's data were hacked
- BUPA, where a rogue employee released 547,000 patients' data including names, dates of birth, national insurance numbers and nationalities
- The NHS ransomware attack - WannaCry - part of a hack on 150 different countries, led to a loss of appointments and cancellations of surgical operations. £100 million is now being invested to build greater security
- During US Senate and Congress committee meetings in April, the Chairman and CEO of Facebook, Mark Zuckerberg, acknowledged the need to protect his 2.1 billion subscribers by making significant changes to the Facebook platform and systems to reduce the risk of unconsented "external" mining of personal data by third party apps

## **Principles of GDPR**

In order to ensure that we are compliant with GDPR, it is helpful to remind ourselves of the principles. Article 5 of GDPR describes six principles applied to the collection or processing of personal data:

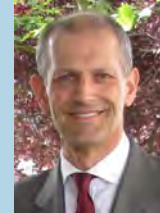
- 1) Personal data must be processed lawfully, fairly and transparently
- 2) Personal data can only be collected for a specified, explicit and legitimate purpose
- 3) Personal data must be adequate, relevant to what is necessary for processing
- 4) Personal data must be accurate and kept up to date
- 5) Personal data must be kept in a form such that the data subject (an identifiable natural person) can be identified only as is necessary for processing
- 6) Personal data must be processed in a manner that ensures its security





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### **GDPR and the pharmaceutical industry**

The pharmaceutical industry extensively uses patient information. This includes regulatory agencies, major pharma, biotech and medical device companies. Pharmaceutical physicians should include the protection and proper use of our patients' private data as part of our professional responsibilities. We should perhaps consider some changes to our code of practice to encompass this regulation.

We have taken advantage of the advances in the use of electronic data collection. Our companies have benefited from the new opportunities of the "Digital Revolution". Genetic and phenotypic analysis of disease have become extremely productive by the use of "big data". These are just a few examples of the technologies underpinning a highly productive period of new medicines development.

The new features of GDPR bring a global reach to control of personal data to anyone resident in the EU member states and affects companies based in any part of the globe. Residency is a broader terminology than citizenship, effectively any individual living in the member states. An "establishment" in the EU, even if the processing itself occurs outside the EU, in theory could be the presence of a single representative of a company or organisation in the EU. It also applies to organisations outside the EU that offer goods or services to individuals in the EU.

For the above reasons, companies based in the USA or Japan may not be exempt to GDPR, despite limited protection of privacy in the USA. The Federal Communication Acts have rules regulating Customer Proprietary Network Information (CPNI). Health data is controlled through Health Insurance Portability and Accountability Act 1996 (HIPAA), the Children's on-line Privacy Protection Act of 1998 and the Fair and Accurate Transactions Act of 2003 (FACTA) are all examples of federal laws. Reflecting diversity of US laws, privacy is enshrined in the Californian constitution. In Japan, the Act on the Protection of Personal Information (Act No. 57 of 2003) (the "APPI") contains similar provisions to GDPR. An act to amend the APPI (the "APPI Amendment") came into force fully on 30 May 2017. The inclusions described within GDPR will therefore capture much of the data collected and stored from global clinical and scientific studies.

### **GDPR preparations for a Pharmaceutical Physician**

In your company, organisation or individual practice there must already be a plan for GDPR compliance. There should already be new procedures in place to deal with GDPR's new transparency and individuals' rights provisions. In a large or complex business this will have had significant budgetary, IT, personnel, governance and communications implications. We

also have advice from the GMC on our responsibilities, particularly when running our own businesses.

GDPR places greater emphasis on the documentation that data controllers must keep to demonstrate their accountability, not simply for collection and storage of data, but also the manner in which the data is processed. A full review and documentation of all private data is essential to demonstrate governance over data and its security. They must review and update documents on all data sharing contracts and other arrangements with external organisations, such as contract research organisations (CROs).

Twelve steps, supplementing the ICO suggestions, to ensure successful application of GDPR:

- 1) Start by looking at your organisation's risk register or draft a risk heat map
- 2) Ensure an audit of all personal data, e.g., where it came from and who you share it with, what it is being used for
- 3) Are the current privacy notices compliant with GDPR implementation?
- 4) Individuals' rights (data subject) - check your procedures to ensure they cover all the rights
- 5) Subject access requests - update your procedures and plan how you will handle requests to take account of the new rules
- 6) Lawful basis for processing personal data - identify the lawful basis for your processing activity in GDPR, document it and update your privacy notice to explain it
- 7) Consent - review how you seek, record and manage consent and whether you need to make any changes and refresh existing consents now if they don't meet GDPR standard
- 8) Children - think now about whether you need to put systems in place to verify individuals' ages and to obtain parental or guardian consent for any data processing activity
- 9) Data breaches - make sure you have the right procedures in place in order to detect, report and investigate a personal data breach.
- 10) Data Protection by Design and Data Protection Impact Assessments (DPIA) - adopt a privacy by design approach and to carry out a Privacy Impact Assessment (PIA) as part of this
- 11) Data Protection Officers - designate someone to take responsibility for data protection compliance and assess where this role will sit within your organisation's structure and governance arrangements
- 12) International - If your organisation operates in more than one EU member state, you should determine and document your lead data protection supervisory authority

## **Some identified special problems for the pharmaceutical industry**

The lawful basis for processing data (Article 6 of GDPR)

At least one of these must apply whenever you process personal data:

- 1) **Consent:** the individual has given clear consent for you to process their personal data for a specific purpose.
- 2) **Contract:** the processing is necessary for a contract you have with the individual, or because they have asked you to take specific steps before entering into a contract.
- 3) **Legal Obligation:** the processing is necessary for you to comply with the law (not including contractual obligations).
- 4) **Vital interests:** the processing is necessary to protect someone's life.
- 5) **Public task:** the processing is necessary for you to perform a task in the public interest or for your official functions, and the task or function has a clear basis in law.
- 6) **Legitimate interests:** the processing is necessary for your legitimate interests or the legitimate interests of a third party unless there is a good reason to protect the individual's personal data, which overrides those legitimate interests. (This cannot apply if you are a public authority processing data to perform your official tasks.)

Some special considerations in the operation of research using individuals' data:

- 1) GDPR replaces the existing data protection framework that exists under the EU DPD and will apply to **any research** that uses personal data, **including privately and publicly funded research.**
- 2) GDPR gives patients (as 'data subjects') more control over their personal data and introduces new and enhanced rights, including the new "right to be forgotten". To which some exemptions are likely in the UK DPA of 2017.
- 3) Companies and CROs that are due to commence clinical studies that will extend beyond May 25 need to be aware now of the changes that GDPR will introduce. They should plan accordingly to ensure that their future clinical trials and research are compliant, and to avoid the need to make retrospective amendments to **consent forms and other clinical trial documentation.**
- 4) Data sent outside the EU for storage and/or processing must be specified in the consent form.
- 5) Protection of personal data regarding EU citizens transferred to destinations outside the European Economic Area must be in a manner that is consistent with how data are protected in the EEA. For example, the European Commission can approve the destination country. The recipient CRO or company may have signed a contract obliging them to protect the personal data; or if the recipient company is located in the USA can be certified under a scheme similar to the EU-US

Privacy Shield Scheme.

## **Conclusion**

This is a brief introduction to GDPR and the impact specific for the pharmaceutical industry. The key actions are audits and analysis of existing data.

Our *Good Pharmaceutical Medical Practice* document holds the pharmaceutical physician accountable for the wellbeing/safety of patients (study participants) and their privacy. Our responsibilities also extend to our colleagues at work (other employees) and organisation with whom we work and their privacy needs. Our training involves detailed analysis and documentation. We should follow these principles with the management of individuals' private information.

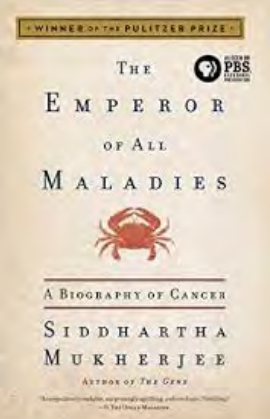
The emphasis of GDPR is on **transparency, security** and the **accountability** of data controllers, whilst standardizing and strengthening the protection of personal data across the EU. In short, the regulation aims to strengthen the rights of individuals so that they are better informed about how their data are to be used, and sets out clearer responsibilities and obligations on healthcare professionals and companies using such data.

Any comments on the GDPR or advice to members of the Faculty can be sent to the Journal and are most welcome.

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[National Data Protection Authorities Justice and Consumers EU](#)  
[ICO self-assessment tool kit](#)  
[European Data Protection Supervisor Data Audit](#)  
[GDPR full text](#)  
[GMC advice on GDPR](#)  
[Good Pharmaceutical Medical Practice and GPMP Support Network](#)

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# BOOK REVIEW

## THE EMPEROR OF ALL MALADIES

BY SIDDHARTHA MUKHERJEE



DR GILLIES O'BRYAN-TEAR

This deep and rich account of the history of cancer and its treatments is quite extraordinary, and utterly unique. It is no surprise it won the Pulitzer Prize.

Written by a (then) young and well respected Assistant Professor of oncology at Columbia, who had been a Rhodes scholar at Oxford and trained at Stanford and Harvard, it is a comprehensive, delicately written and fascinating account of cancer, from the earliest descriptions of "bulging tumours on the breast" by the Egyptian physician Imhotep, who lived in 2625 BC, to the most modern precision medicine of the early 21st century. It grips you from the first page of the Prologue: "On the morning of May 19, 2004, Carla Reed, a 30-year-old kindergarten teacher from Ipswich, Massachusetts, a mother of three young children, woke up in bed with a headache". Mukherjee draws you in with wonderful language and real-life accounts of this disease, drawn from his own experience. "In the brief span between 1846 and 1867, two discoveries swept away these two quandaries that had haunted surgery...". The two quandaries were of course sepsis and pain, and the two discoveries were carbolic acid (Pasteur/Lister) and ether (William Morton, a Boston dentist) – antiseptics, and anaesthesia.

So this book is not just about cancer, it embraces the history of medicine, the history of surgery, and much besides. Mukherjee recounts a number of historical curiosities: for example, Lister had observed sewage workers cleaning out their waste with a cheap, sweet-smelling liquid called carbolic acid. A fascinating insight into one of the greatest breast cancer surgeons in history, William Halsted: he was a life-long opiate addict who kept it under control by rigorous self-discipline. He was ascetic, ran gruelling surgical residency programmes, and was almost messianic in the relentless energy with which he attacked breast cancer. Noticing that recurrences were all too common, locally in the neck, in the nodes, and in the axilla, and in the chest wall, he undertook increasingly radical surgery, which eventually became mutilating and in some ways worse than the disease he was trying to eradicate. He went further and further: "a macabre marathon was in progress" as his students and he took more and more of the mediastinum, the entire pectoralis major, parts of the collar bone, in their relentless pursuit.

This became such orthodoxy that it took years to prove that you did not need to undertake such radical surgery on all women, since many tumours were too small to need it. It took years of painstaking long-lasting controlled trials in the 1970's by an Italian breast surgeon, Umberto Veronesi, to show that breast conserving surgery had, in many cases, as good a result as radical mastectomy, when combined with local radiotherapy and later, excision of nearby nodes. This would mean that many thousands of women would be spared this horrible mutilation. But there was massive and concerted opposition to this, then heretical, approach, which took a decade to gain acceptance until the New England Journal of Medicine published study results in 1981.

Mukherjee describes the Nixon-led explosion of funding for cancer research in the early 1970's, which had been kick-started by a searing full-page advertisement in the Washington Post, in which Dr Sidney Farber said: "We are so close to a cure for cancer. We lack only the will and the kind of money and comprehensive planning that went into putting a man on the moon". Sidney Farber had been a friend of the wealthy socialite Mary Lasker throughout the 1950's and 1960's, campaigning tirelessly for the cause of cancer research funding (Lasker's husband had died of colon cancer). There followed a huge government and donor led increase of funding for cancer research, which funded the building of the Dana Farber Hospital in Boston, amongst many other hospitals and departments. There is a wonderful historical description of the brave pioneers of chemotherapy, which was a terrifying treatment at first, by Farber in Boston, and by DeVita, Frei and Freireich at the National Cancer Institute. Out of this was born the first curative chemotherapy trials for choriocarcinoma, the MOPP and VAMP protocols for Hodgkin's disease (and other lymphomas), and the first treatments of childhood and adult leukaemia: there is a moving account of the early setbacks, and finally the first cured child, still alive today.

This is a beautifully written book, as exemplified here, on the first use of linear accelerators in lymphomas by Henry Kaplan, a Stanford radiologist: "the powerful oculus of Kaplan's intellect, swivelling about through the malignant world, ultimately landed on the most natural target for his investigation: Hodgkin' disease." His elegant prose binds this wide-ranging story into a uniform whole.

However, the story neglects the great contributions to the "war on cancer" from outside the US, with the notable exceptions of the UK statistician Bradford Hill (who conducted the first randomised controlled trial of streptomycin in tuberculosis) and Veronesi. For example, the UKALL leukaemia research programme in the UK, a massive multi-study and multi-year programme which led to real advances in the treatment of childhood leukaemia, does not get a mention. With that criticism aside, this is a noble and important work, essential reading for anyone involved in, or interested in the treatment of cancer in particular or medicine as a whole. It is completely accessible to the lay reader, whilst providing easily enough interesting and historical technical detail to satisfy the most inquisitive oncologist. My highlight would be the explosive funding of cancer research in the USA in the 1970's which led to many important breakthroughs, including the first use of chemotherapy in leukaemia and the first cure: this reminds us all of the necessity for funding, the power of such a great nation to effect change in such an important area, and the duty of all of us to support that effort throughout the world. The EU research funding programmes, like Horizon 2020, are important successors to that effort, and can now stand beside the US effort in scale and reach.

# Feedback and ideas for Edition 3

We would really value your feedback and comments on this new format for the FPM Newsletter.

The next edition of the Journal is on paediatric medicines. Please let us know if you would like to contribute.



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