

# PP

PHARMACEUTICAL **PHYSICIAN**

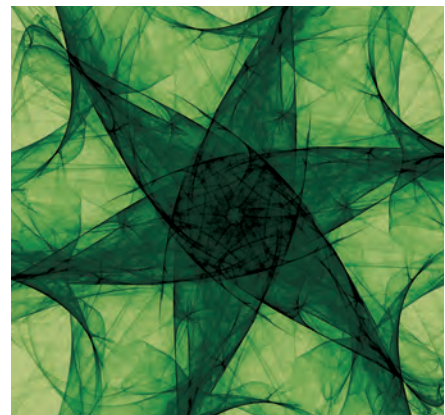
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REGULATORY ROUND UP

### Special features

Meeting report - 10th  
BrAPP Education Day

Personal Development -  
Developing Resilience  
Using Mindfulness at  
work



APRIL 2018 **VOLUME 28 | SPRING**



JOURNAL OF THE BRITISH  
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PHYSICIANS



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<b>Medical Director Early Clinical Research</b> Research Organisation – Respiratory/ Infectious Diseases	Central London	PP 6882
<b>Principal Investigator – Early Clinical Research</b> Research Organisation – Respiratory/ Infectious Diseases	Central London	PP 6951
<b>Medical Monitor</b> Emerging Biotech – Pivotal phase II / III EU clinical trials	Central London	PP 7054

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PHARMACEUTICAL **PHYSICIAN**



APRIL 2018 **VOLUME 28 | SPRING**

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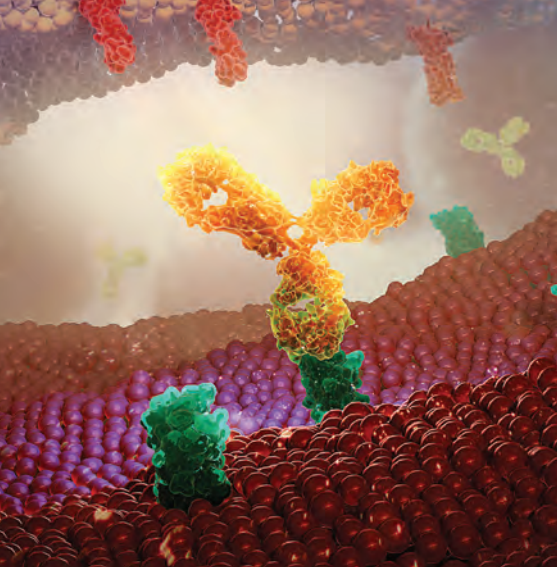
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Senior Pharmaceutical Physicians and Scientists – UK, US

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WELCOME TO A Spring issue of Pharmaceutical Physician. We live in interesting and changing times – the weather in the UK is but one example of this and we have experienced two SSW events so far in 2018 – Sudden Stratospheric Warming for the non-meteorologically minded amongst you. The first caused London (and yes, other and most parts of the country were much more severely affected) to be plunged into a picturesque but treacherous city and it even snowed inside (not around or blown in from the outside) the canopy of Paddington Station such were the weird atmospheric conditions. Nevertheless the turnout for Session 2 of the PostGraduate Course in Pharmaceutical Medicine was 100% and it is probably true that a degree of adversity brings out the best in us. They are all to be congratulated for their fortitude.

The direction of the April issue of PP is to continue the theme of improvement through experience and learning. We have two articles which may help each and every one of us respond to workplace challenges and feel more involved and yet more content. Sharon Leighton looks at developing resilience through mindfulness. And Liz Clark reports on attending a charisma workshop where she was forced to reflect how we present ourselves in life and the benefits of thinking about how others might receive those messages.

Tributes are also paid to two contributors to the advancement of pharmaceutical medicine. Dr Joe Chiesa, a familiar face at BrAPP and Faculty meetings and a doyen to the importance of the training of pharmaceutical physicians is remembered by his most recent work colleagues at TranScrip Partners and also by a friend and former colleague, Dr David Blowers. Also, Peter Jay could certainly be described as a character in our midst. The identification and detection of clinical trial fraud is of paramount importance to the industry and not least to patients. Peter as a retired senior policemen was very adept

at “smelling a rat”. Dr Jane Barrett who worked closely with him offers her recollections.

The bulk of this issue is a detailed and fascinating report of our 2017 BrAPP Education Day. Drs Barden, Chukwujindu, Carrasco and Sheth provide their reflections on another super day. It was also the occasion upon which BrAPP celebrated its 60th birthday. A global landmark for associations of doctors working in the pharmaceutical industry. Pictures of the day will soon be available on the new BrAPP website which will be launched later in April.

Change and development are inevitable factors in life and at BrAPP we need to respond to the needs of our members and their colleagues. For the foreseeable future, we plan to reduce the frequency of Pharmaceutical Physician from six to four times per year. Authors are increasingly finding article creation challenging. However, we also plan to communicate with you more frequently via email and sometimes social media – we are currently reviewing our policy! The advent of GDPR (General Data Protection Regulation 2018) will require us to continue to protect your data as before. Please be assured that we never give member or subscriber data to any other person or organisation without express permission.

Communication and networking are of great importance to us and we hope to you too and so we are seeking ways to enhance our communication strategy. If you have any thoughts or ideas as to how we might do things better, please feel free to get in touch.

APRIL 2018

EDITORIAL



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## 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](mailto:info@envigo.co.uk). ANNE HETHERINGTON, SENIOR REGULATORY CONSULTANT



ENVIGO.COM



Anne Hetherington

### EUROPEAN MEDICINES AGENCY (EMA)

News and press releases

- News and press releases: *EMA's Business Continuity Plan for Brexit published*
- News and press releases: *Raising awareness of the perils of antimicrobial resistance*
- News and press releases: *EU scientific opinion: how to assess progress on reduction of antimicrobial resistance and antimicrobial consumption*
- News and press releases: *Reporting side effects of medicines*
- News and press releases: *Unparalleled access to clinical data - one year on*
- News and press releases: *New action plan to foster development of advanced therapies*
- News and press releases: *EMA takes yet another step in public engagement with its first public hearing*

Updates

- Scientific guideline: *Concept paper on predictive biomarker-based assay development in the context of drug development and lifecycle*, draft: consultation open
- Scientific guideline: *Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products - Revision 1*, adopted
- Scientific guideline: *Concept paper on the revision of the guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells - Superseding document*, draft: consultation open
- Scientific guideline: *Reflection paper on promotion of pharmacovigilance reporting*, adopted (updated)
- Scientific guideline: *Draft ICH E9 (R1) addendum on Estimands and sensitivity analysis in clinical trials to the guideline on statistical principles*

# 4

for clinical trials, step 2b - Revision 1, draft: consultation open

- Scientific guideline: *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 pulmonary disease due to Mycobacterium tuberculosis - Revision 1*, adopted
- Scientific guideline: *Reflection paper on the pharmaceutical development of medicines for use in the older population - First version*, draft: consultation open
- Regulatory and procedural guideline: *Guideline on good pharmacovigilance practices (GVP) - Product- or population-specific considerations IV: paediatric population*, draft: consultation open
- Regulatory and procedural guideline: *Comments received from public consultation on good pharmacovigilance practices (GVP) - GVP Module VI – Management and reporting of adverse reactions to medicinal products (EMA/873138/2011 Rev. 2)*
- News and press releases: *Science and innovation for better medicines*
- News and press releases: *Involving young people in EMA activities*
- Newsletter: *What's new in pharmacovigilance - QPPV Update - Issue 2 - 2017*
- Regulatory and procedural guideline: *External guidance on the implementation of the European Medicines Agency policy on the publication of clinical data for medicinal products for human use (version 1.3)*, adopted
- Scientific guideline: *Guideline on clinical investigation of medicinal products for the treatment of chronic*

*heart failure - Revision 2*, adopted

- Scientific guideline: *Guideline on clinical investigation of new medicinal products for the treatment of acute coronary syndrome - First version*, adopted
- Scientific guideline: *Guideline on the clinical investigation of medicinal products for the treatment of axial spondyloarthritis - Revision 1*, adopted
- Scientific guideline: *Draft guideline on the clinical evaluation of medicinal products indicated for the prophylaxis or treatment of respiratory syncytial virus (RSV) disease*, draft: consultation open
- Scientific guideline: *Draft guideline on clinical investigation of recombinant and 4 human plasma-derived factor VIII products*, draft: consultation open
- Scientific guideline: *Reflection paper on the use of extrapolation in the development of medicines for paediatrics*, draft: consultation open
- Scientific guideline: *ICH guideline E18 on genomic sampling and management of genomic data - First version*, adopted
- Scientific guideline: *Guideline on good pharmacovigilance practices: Module XV – Safety communication (Rev. 1)*, adopted (updated)
- Scientific guideline: *Guideline on good pharmacovigilance practices (GVP) - Module VIII – Post-authorisation safety studies (Rev. 3)*, adopted (updated)
- Scientific guideline: *Guideline on good pharmacovigilance practices: Annex I - Definitions (Rev. 4)*, adopted (updated)
- Scientific guideline: *Guideline on good pharmacovigilance practices (GVP): Module IX – Signal management (Rev. 1)*, adopted

## REGULATORY ROUND UP



Overview of comments received on 'Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products', adopted

Overview of comments received on draft Guideline on clinical investigation of medicinal products for the treatment of chronic heart failure (CPMP/EWP/235/95, Rev.2)

Overview of comments received on 'Guideline on clinical investigation of new medicinal products for the treatment of acute coronary syndrome'

### MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA)

- *MHRA and making a success of Brexit*
- *BIA & MHRA publish report 'Innovation in life sciences in a changing and dynamic environment'*

### FOOD AND DRUGS ADMINISTRATION (FDA)

- *FDA develops rapid and sensitive assay to assess antibody response to Ebola virus vaccine without using the virus*

## REGULATORY ROUND UP



▶▶ Continued from page 5

- *FDA approves Vabomere (meropenem and vaborbactam), a new antibacterial drug*
- *Antibacterial Therapies for Patients With an Unmet Medical Need for the Treatment of Serious Bacterial Diseases*
- *FDA develops a novel biomarker based test that improves ability to identify asymptomatic carriers of malaria*
- *FDARA: Making a Difference for Industry and Patients*
- *FDA Press Release: FDA improves access to reports of adverse drug reactions*
- *Expedited Programs for Serious Conditions—Drugs and Biologics Guidance for Industry*
- *E9(R1) Statistical Principles for Clinical Trials: Addendum: Estimands and Sensitivity Analysis in Clinical Trials Guidance for Industry*
- *Pediatric Gastroesophageal Reflux Disease: Developing Drugs for Treatment Guidance for Industry*
- *Respiratory Syncytial Virus Infection: Developing Antiviral Drugs for Prophylaxis and Treatment Guidance for Industry*

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PHARMACEUTICAL **PHYSICIAN**

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# Power to the Patient

## WHAT?

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- pH Associates ([www.phassociates.com](http://www.phassociates.com)) is an OPEN Health company ([www.OPENhealth.co.uk](http://www.OPENhealth.co.uk)).

## WHY?

- Delivering patient centred evidence from early drug development to late stage use is now a requirement for all stakeholders.
- To establish long-term successful medicines, today's pharma professional needs more than data.
- Work with us to measure how a patient is feeling and to understand the actual impact of treatment or disease on daily life.

## HOW?

**Our PCO consultants**, with expertise in measuring the patient perspective, partner with our clients to:

1. Optimise patient centred measurement **strategy**.
2. Collect the right patient centred **data** at the right time.
3. Turn data into patient centred **value messages**.



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# MEETING REPORT: BrAPP Education Day:

05 December 2017

Report by Drs Rob Barden, Carlos Carrasco, Kamlesh Sheth and Joy Chukwujindu



THE 10TH BRAPP EDUCATION DAY OFFERED MEMBERS AND COLLEAGUES AN INSIGHT INTO SOME OF THE MOST EXCITING DEVELOPMENTS IN GENE THERAPY AS WELL UPDATES ON REGULATORY, COMPLIANCE AND SAFETY ISSUES



## CAR T-CELL THERAPY IN HAEMATOLOGICAL MALIGNANCIES

**PROFESSOR DAVID LINCH, PROFESSOR OF HAEMATOLOGY, UCL**

Professor David Linch gave a very comprehensive and insightful presentation on this exciting and complex state-of-the-art therapy.

He set the scene by stating that there was still a considerable 'unmet clinical need' even in the treatment of

relatively good risk malignancies such as Acute lymphoblastic leukaemia (ALL) and Diffuse large B-cell lymphoma (DLBCL), with survival being considerably reduced the later the age at onset. In children and young adults, even though the 5yr survival is high, post relapse results are poor. Also many patients are deemed unsuitable for transplantation due to uncontrolled disease, with survival post-transplant relapse being very poor.



CREDIT: EYE OF SCIENCE/SCIENCE PHOTO LIBRARY

**CAPTION: COLOURED SCANNING ELECTRON MICROGRAPH (SEM) OF A CANCER CELL (GREEN) BEING ATTACKED BY A CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL (PINK). THE BREAST CANCER CELL IS UNDERGOING PROGRAMMED CELL DEATH, OR APOPTOSIS, WHICH HAS BEEN INDUCED BY THE CAR T-CELL. CAR T-CELLS ARE CELLS FROM A PATIENT'S IMMUNE SYSTEM THAT HAVE BEEN EXTRACTED AND MODIFIED TO RECOGNISE AND ATTACK THE PATIENT'S CANCER CELLS, BEFORE BEING REINTRODUCED TO THE PATIENT. MAGNIFICATION: X3,660 WHEN PRINTED AT 10 CENTIMETRES WIDE.**

# 8

Treatment of haematological malignancies involving the immune system using T-cell directed depletion commenced in 1956 with Barnes and Loutit's mouse model concept of 'graft versus leukaemia' and has since evolved into the contemporary genetic engineering of T-cells initially involving the creation of new T-cell specificities such as T-cell receptors (TCRs) and more recently Chimeric antigen receptors (CARs) using 'Adaptive Cell Transfer' technology, with the 3 key success factors being related to CAR T-cell production, Vector anatomy and Lymphodepletion.

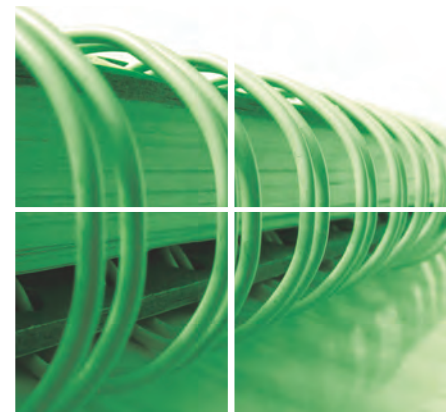
CARs are engineered receptors which are derived from monoclonal antibodies. They consist of 2 main components – an intracellular TCR signalling component (Endodomain) which is the functional end of the receptor and an extracellular antigen recognition region, often antibody derived from immunoglobulin chains, (Ectodomain), this being the recognition end of the receptor. They are linked through the cell membrane (Transmembrane domain).

The extracellular antigen recognition region targets and binds onto specific tumour associated antigens, the one most commonly targeted to date being the CD19 antigen, which are found on malignant B-cells (and also healthy cells).

1st generation CARs had a relatively simple intracellular domain from endogenous TCRs (CD3-zeta chain), with little evidence of anti-tumour activity. 2nd generation CARs possess an additional costimulatory domain (e.g. CD28), thereby providing additional signals to the T cell, with 3rd generation CARs progressing to possess 2 costimulatory domains (e.g. CD28 + OX40), to further augment potency and to improve their expansion and persistence. [See Figure: The Development of CARs]

The art of CAR T-cell production is shrouded in secrecy, but essentially starts with the removal of white cells from the patient by leukapheresis, which are then taken to a specialist production facility where the T-cells are activated and genetically engineered.

**MEETING REPORT:**  
**BrAPP Education Day:**  
 05 December 2017

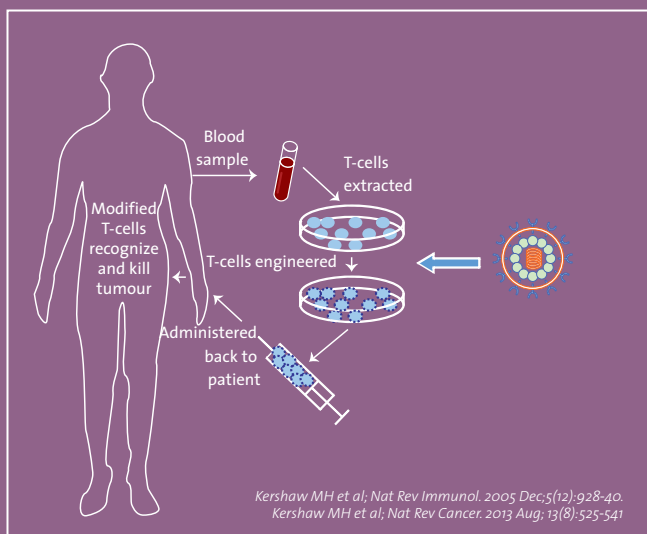


Currently this is most often facilitated by using a viral vector (e.g. retrovirus) to transfer the coding sequence, so that it is expressed in CARs which are specifically directed towards antigens on the patient's own tumour cells. These genetically engineered CAR T-cells are then expanded under various conditions and harvested. Finally, they are re-infused into the patient, who will have undergone a preparative lymphodepletion prior to the re-infusion. This whole process can take around 17 days. [See Figure: Adoptive Immunotherapy with Engineered T-cells].

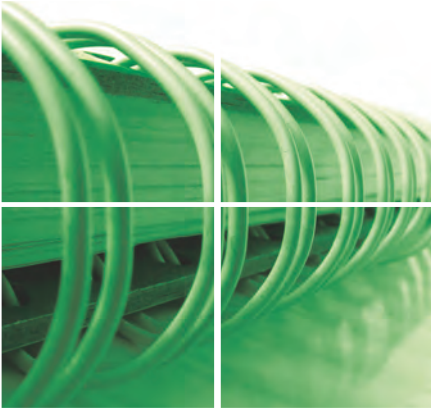
There is a need to lymphodeplete the patient prior to reinfusion of the genetically modified CAR T-cells. This is commonly achieved with fludarabine and cyclophosphamide.

Most early studies resulted in poor persistence of the infused CAR T-cells, showing only transient efficacy, but minimal toxicity, aside from the need to manage the depletion of normal B-cells. However more recent studies using 2nd and 3rd generation CARs, mainly in patients with ALL and DLBCL, have shown much improved overall response rates (Partial response + Complete

**FIGURE 1: Adoptive Immunotherapy with Engineered T-cells**



Continues on page 10 ►►



»» Continues from page 9

response), with increasing relapse free survival. But as these cells are not cleared from the body quickly, as well as causing normal-cell depletion, they often show characteristics such as cytokine release syndrome (CRS) early on or neurotoxicity such as encephalopathy. CRS is currently treated with short course steroids (but these may compromise the persistence of the CAR T-cells) and IL-6R antagonism using tocilizumab. One further possibility is to engineer a 'suicide gene' into the modified CAR T-cells.

The FDA have recently approved the first two CD19 targeted CAR therapies. Kymriah (tisagenlesleucal; Novartis) is now licensed in the US for use in relapsing/refractory B-cell precursor ALL and Yescarta (axicabtagene ciloleucel; Kite/Gilead) for use in relapsing/refractory DLBCL.

Prof Linch mentioned the 4th Hurdle challenges ahead for both products in respect of their gaining NICE approval, given their respective high cost of goods, even at a QALY threshold of £50k.

He closed by stating that CAR T-cell therapy was still only in its infancy and that today it is only used in end-stage patients, but posed the question – "What of tomorrow?"

### CURRENT TRENDS IN CANCER IMMUNOTHERAPY

**SPEAKER: MIKE HOLMES MD FRCS**

*Overview:*

Advances in immunotherapies for cancer have propagated new treatments that trigger the immune system to effectively respond and attack tumours, delivering dramatic benefits to patients who suffer with cancer. Dr Mike Holmes MD FRCS, Executive Director of Oncology for Medical Affairs in Europe and Canada, MSD - presented a fascinating historical timeline on how a century (1890-1990) of immunological research into cancer was marginalised and blatantly ignored by the scientific community. Regardless of various

seminal immunological advances, immunotherapy, as a means towards treating cancer failed to flourish and gain any momentum. Mike summarised and collated key stories from several investigators who performed these ground-breaking experiments and established the frontiers of cancer immunotherapy. Today more recent immunological breakthroughs have catapulted this once ostracised science into the limelight generating a momentous surge and shift towards the premise that this therapy – could just be – the beginning of the end of cancer. These are exciting times for cancer immunotherapy. After many years of disappointing results, the tide has finally changed and immunotherapy has become a clinically validated treatment for many cancers and other autoimmune diseases. Mike then presented how such key immunological discoveries led to the generation and launch of new medicines unleashing the immune system's ability to attack tumours and halt the spread of cancer.

### TOXIC BACTERIA, MAGIC BULLETS, CANCER IMMUNITY CYCLE TO THE GLOBAL PHARMACEUTICAL MANUFACTURING OF CTLA-4 AND PD-1/L1: IMMUNOLOGICAL EVOLUTION TO REVOLUTION OF CANCER TREATMENTS.

Coley's Toxin and Ehrlich's 'magic bullet' concept'

Mike initiated his presentation by introducing and conveying the captivating life story of the widely regarded "father of immunotherapy" – William B. Coley (1862-1936). In the 1890s, this bold clinician-scientist plunged a syringe loaded with living *Streptococcus pyogenes* into an inoperable obstructive tumour at the base of a drug addict's neck – simply on a hunch that severe infection could cause cancer to regress. His hunch was based off of 47 scant patient profiles and an obsession into one particular case, according to the medical literature, that found this doctor frantically scouring the ghettos in New York city where an alleged German immigrant, who seven years prior with terminal

cancer, had been found cancer-free solely after contracting a widespread erythematous superficial skin infection, i.e. erysipelas, caused by beta-hemolytic group A Streptococcus bacteria. Mike stressed to the audience that was all Coley needed to proceed directly to human trials, and the infamous drug addict named Zola would become his first test subject.

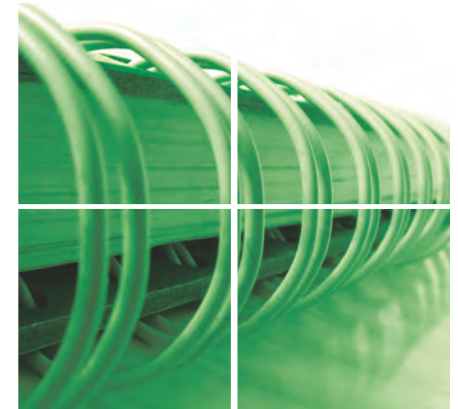
Advancing twenty years past this initial event (i.e. 1910), Mike then went on to describe Paul Ehrlich's, German Nobel Laureate and 'founder of chemotherapy' (1854-1915), 'magic bullet concept' which postulates the ability to engineer and create 'targeted cell-structure based-medical therapies' to attack pathogens; whilst, remaining harmless within healthy tissues. Ehrlich was able to base such theories on his beliefs and was the first to coin the phrase 'receptors'. He believed that these so-called 'receptors' bound and had affinity towards antigens. Moreover he hypothesized that these receptors are either associated with cells or were dispersed widely throughout the blood stream in response to antigen interactions. Ironically, all of these beliefs were built

upon his experiences in the treatment of infectious diseases with drugs derived from the German dye industry. Thus chemical dyes were the catalyst and foundation for early chemotherapy usage in man.

### The Cancer Immunity Cycle

As surgical resection, chemo- and radiotherapy gradually evolved to become the cornerstone and main treatments for cancer management; further elucidation into the pathophysiology of cancer immunity and T cell biology progressed, albeit in separate and divergent paths. Mike next focused his presentation on the seven pathophysiological steps that cancer utilises to evade the escape of the immune system.

1. Release of cancer cell antigens (cancer cell death)
2. Cancer antigen presentation
3. Priming and activation of T cells
4. Trafficking of T cells to tumours
5. Infiltration of T cells into tumours

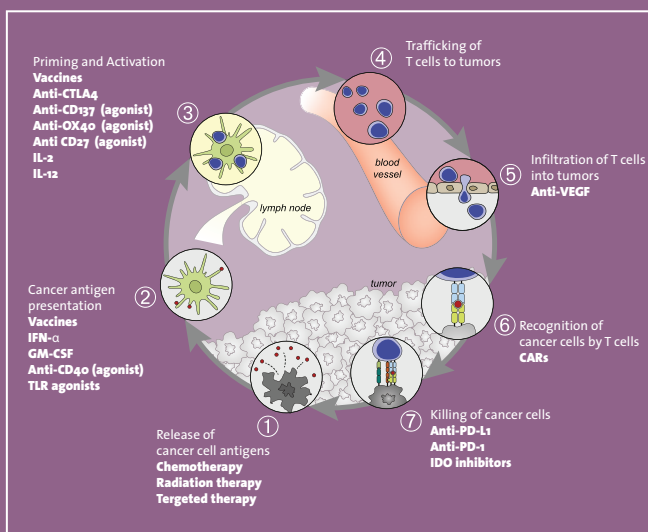


6. Recognition of cancer cells by T cells
7. Eventual killing or destruction of the cancer cells.

*Reviewed in: Chen and Mellman Imm. Rev 2013*

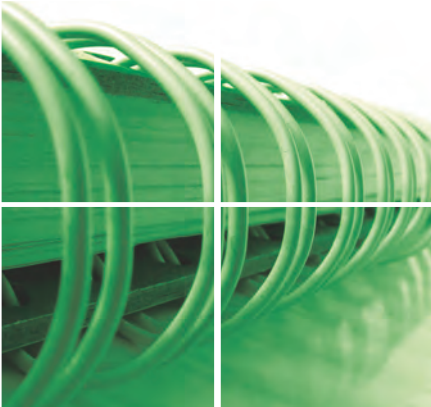
Mike explained that the cancer immune cycle and its cellular interactions are complex. Nevertheless, he described the steps of the cycle (i.e. key immune cells and key effective molecules) in a clear and comprehensive fashion. Moreover, he stressed that ongoing research and clinical trials are advancing our knowledge into the molecular and cellular intricacies that encompass cancer medicine. This knowledge has supported principal investigators by identifying crucial targets/checkpoints such as CTLA-4 and PD-1/L1. Tumours selectively express CTLA-4 in peripheral lymph node tissue, whilst PD-1 is expressed in a variety of immune cells. Biologics, monoclonal antibodies, with an affinity towards these immune regulators have shown their effectiveness at disrupting a cancer cell's ability to evade immune surveillance allowing patients the ability to mount an effective immune response. Inhibition of either CTLA-4 or PD-1/L1 has culminated in the pharmaceutical

**FIGURE 2: The Cancer Immunity Cycle**



**MEETING REPORT:**  
BrAPP Education Day:

05 December 2017



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manufacture and administration of these immunotherapies for melanoma, non-small cell lung cancer (NSCLC), and other cancers.

Mike indicated that CTLA-4 was the first immune checkpoint receptor to be clinically targeted. Ipilimumab (Bristol-Myers Squibb, Princeton, NJ), an inhibitor of CTLA-4, is approved for the treatment of advanced or unresectable melanoma. He presented Ipilimumab's impactful pooled survival analysis from Phase II/III trials in advanced melanoma. He then conveyed that hundreds of clinical trials on anti-PD-1/L1 mAbs are under active development. Some of them have entered phase 3 clinical trials and are benefiting many patients.

Pembrolizumab (Keytruda® injection, MSD) is a high-affinity, humanized IgG4 PD-1 blocking antibody approved by the FDA and the EU is licensed for renal cell carcinoma, NSCLC, HNSCC (head and neck squamous cell carcinoma) and bladder (urothelial) cancer.

Mike summarised his presentation with the future developments in cancer immunotherapy.

- Re-exploring therapeutic limits – combination strategies (> 80 under investigation)
- Novel immune checkpoint targets and modulators (T cell has > 200 receptor types)
- New biomarkers to help target therapies
- CAR-T cell therapy
- Bispecific antibodies
- Individualisation in mouse xenografts
- Blood based biopsies including cfDNA signatures

**EARLY ACCESS TO MEDICINES (EAMS) SCHEME**

**DR ZAHID BASHIR OF OMNIAC PHARM CONSULT LTD**

Industry has made great progress in making life-saving treatments available for several hundreds of conditions. However there remain numerous life-threatening and chronically debilitating conditions for which there are no

“ THERE REMAIN NUMEROUS LIFE-THREATENING AND CHRONICALLY DEBILITATING CONDITIONS FOR WHICH THERE ARE NO LICENSED TREATMENTS AVAILABLE. ”

licensed treatments available. There are many compounds in the Industry's pipeline, some of them with great potential, to address this unmet need. The issue is; patients with life-threatening conditions don't have time to wait for these compounds to complete the full clinical development and regulatory processes before being made available by regular access channels.

One way to access these promising unlicensed medicines is by participating in clinical trials; however not all patients are eligible for ongoing clinical trials. They access unlicensed medicines by mechanisms known by a plethora of terms – managed access programmes, early access, expanded access, named patient use, and compassionate use. Confusing?

Dr Zahid Bashir of Omnicom Pharm Consult Ltd cleared the confusion in his very engaging lecture on his experience of Early Access to Medicines (EAMS) scheme in the UK at the recent BrAPP education day. Use of prescription-only medicines prior to grant of marketing authorisation by competent authorities is

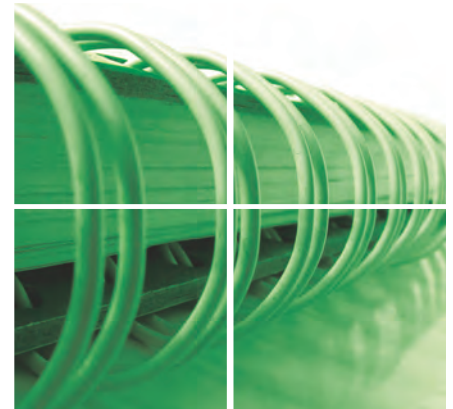
known as unlicensed medicine use. The legal basis of such a use is Article 5 Directive 2001/83 EC, for an individual patient and article 83 Regulation 726/2004/EC for cohort of patients. Different member states have implemented this differently and so far, France was the only state to have successfully implemented successful cohort access to unlicensed medicines – ATU.

In the UK, EAMS was launched in April 2014 with the aim to give patients with life-threatening or seriously debilitating conditions access to medicines that do not yet have marketing authorisation when there is a clear unmet medical need. Dr Bashir explained that EAMS is not a substitute for appropriate clinical development and is primarily aimed at medicines towards the end of their development

There are four main stakeholders in the five-step EAMS process (*Fig 3. - below and Fig 4. - page 14*). The first step is Promising Innovative Medicine designation, which is generally based on phase II or phase III data.

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Once the PIM designation is obtained, the company can ask for a pre-submission meeting with MHRA and apply for the next step i.e. scientific opinion. The EAMS dossier follows the Common Technical Dossier (CTD) format. MHRA has a 75 -90 day process and issues a scientific opinion (SO) taking into consideration the benefit:risk. This opinion is valid for one year and the company can apply for renewal. Whilst PIM decisions are not publicised by MHRA, the SO are published on the MHRA website.

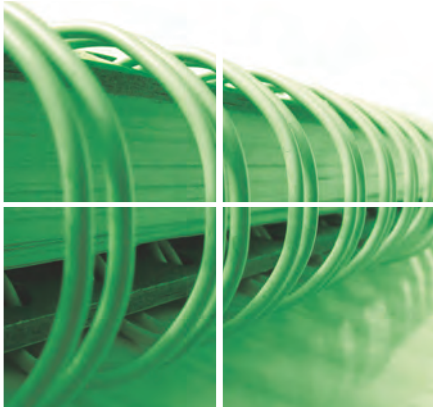
The next step is implementation in collaboration with NHS England and the company needs to make the drug available free of charge until the Marketing Authorisation is granted. This is different from the French ATU programme where the ATU drugs are reimbursed. This is one of the potential downsides of the scheme for pharmaceutical companies. However, there are indeed several advantages for the companies: creating goodwill amongst health professionals and patients by making innovative medicines for conditions with real unmet medical need, opportunities for data collection for NICE submission. In addition, the baseline commissioning for EAMS

**FIGURE 3:** The EAMS process (1)



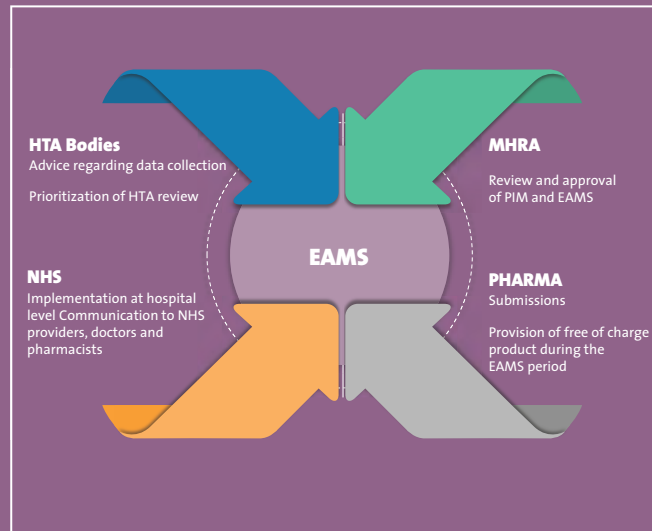
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**| FIGURE 4: The EAMS process (2)**



medicines (following positive NICE guidance) is reduced to 30 days (usually 3 months).

Dr Bashir emphasised the importance of having a clear exit strategy for the companies especially in cases where the NICE decision is negative.

In summary, this was a truly engaging lecture by Dr Bashir who shared his experience of the UK EAMS and clarified the process as well as pros and cons of EAMS.

### SETTING THE STANDARDS FOR THE PROMOTION OF MEDICINES

**ETTA LOGAN,  
DEPUTY DIRECTOR PMCPA**

Etta gave yet another useful topical presentation in relation to PMCPA activities, majoring on the PMCPA's findings from audits entitled 'Learning from audits'.

Learning from audits:

Etta set the scene by pointing out that 3 audits had already been arranged for 2018, suggesting that they appeared to be coming more prevalent!

Audits are usually requested by either the Code of Practice Appeal Board as a Code ruling sanction or by the ABPI Board to assist in deciding whether to suspend or expel a company from the ABPI. A company may also request a voluntary audit!

For those of who have not had the dubious pleasure of participating in a PMCPA Audit, Etta started by outlining the procedure. This starts with the Authority requesting that the company provides them with certain materials for examination prior to their visit - these often include specific items which were associated with the circumstances which gave rise to the audit. The Authority audit team normally consists of 2-3 members. A list of individuals required to attend for confidential interviews (including staff from European HQs) is drawn up by the audit team. The requested materials are examined in depth. Company procedures are reviewed and discussed. The visit may last 2-3 days, with a report with recommendations being sent to the company shortly after the visit. The company comments on the report, usually be specifying how it will

actively address the Authority's recommendations, the objective being to avoid the Appeal Board requesting the need for a re-audit!

So what are the major learnings?  
*[See panel: Audits – Learning topics]*

Leadership comes from the top, including the Board & CFO.

Have a company culture which encourages staff to be responsible & accountable, also it operates in a transparent environment which actively encourages debate.

Share Good Compliance Practice – very important.  
Actively incorporate the commercial division into the company compliance infrastructure, potentially by them being involved with setting compliance objectives and also placing them in Signatory roles.

Medical reviewers/signatories should have sufficient standing within the company and also develop a sound professional relationship with commercial colleagues, ideally built on

mutual respect for each other's roles and associated responsibilities.

Company Code Procedures SOPs should be readily accessible, with staff being regularly trained on them, such that they have an adequate up to date working knowledge of them, which will enable them to carry out their role in a fully code compliant way.

Code practices within the company should be carefully monitored to identify areas of non-compliance and also errors of process or decision-making, with a learnings system in place.

Simple solutions, such as Signatories monitoring each other, may provide compliance alignment checks.

In respect of compliance psychology, this should enable the company to do business more compliantly, often involving management getting to know their staff, with the individual ultimately seeing compliance as a personal challenge.

Financial controls relate to ensuring that the annual PMCPA 'Disclosure' details are complete and correct, particularly in relation to 'Transfer of Value' returns.

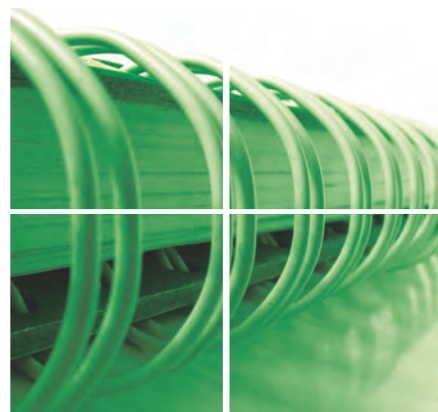
Compliance risks may originate from 'Whistleblowers' and also from not carrying out due diligence on 3rd parties on appointment and thereafter not managing their use of subcontractors and control of materials. Measures should be in place to manage known compliance risks.

Case Reviews published 2017 - PI safety update issue:  
Etta pointed out that reviewers & Signatories should be particularly vigilant in checking that the PI had been updated to reflect any safety-related updates contained within the Summary of Product Characteristics.

What else is PMCPA up to?:  
Etta informed us that they are working with the 'Compliance Network' on a

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new guidance document relating to the approval of meetings/meeting arrangements for meetings held outside the UK. They are also updating their guidances relating to Clause 3 and Digital communications.

## PHARMACOVIGILANCE CURRENT THINKING

DR KRISTINA STRUTT

**ADVERSE DRUG REACTION (ADR)** definition covers both authorised use of a medicinal product and its use outside of the terms of the marketing authorisation. It is a response to a medicinal product which is noxious and unintended and may arise from use of the product within or outside the terms of the marketing authorisation or from occupational exposure. Use outside the marketing authorisation includes off-label use, overdose, misuse, abuse and medication errors. Off-label use: situations where the medicinal product is intentionally used for a medical purpose not in accordance with the terms of the marketing authorisation. Misuse: situations where the medicinal product is intentionally and inappropriately used not in accordance with the terms of the marketing authorisation. In practice there are

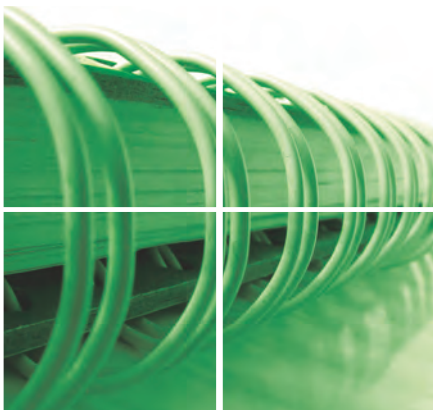
### AUDITS - learning topics

- Leadership
- Company culture
- Good Compliance Practice
- Commercial engagement
- Medical aspects
- Company Code Procedures SOPs
- Training
- Monitoring
- Simple solutions
- Compliance psychology
- Financial controls
- Compliance risks

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challenges with identifying, coding and assessing 'special situations' reports for example determining when a prescriber's action is intentional or not.

**EXPEDITED REPORTING:** All suspected ADRs will now be submitted electronically to EudraVigilance only. Serious ADRs to be submitted within 15 days; Non-serious ADRs (EU only) within 90 days; fully functional EudraVigilance went live on 22nd November 2017.

**SIGNAL DETECTION & RISK IDENTIFICATION:** a signal is information arising from one or multiple sources, including observations and experiments, which suggests a new potentially causal association, or a new aspect of a known association between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action. Signal detection is the process of looking for and/or identifying signals using data from any source. For the purpose of monitoring data in the EudraVigilance database, only signals related to an adverse reaction shall be considered.

MAH is required to monitor EudraVigilance data as part of global signal detection activities. MAH is required to inform competent authorities if new risks or changed risks or changes to risk/benefit balance have been detected.

The requirement for MAH to monitor EudraVigilance data and inform the Agency and national competent authorities of validated signals will enter into force on 22 February 2018 and will only apply, for a transition period, to active substances contained in medicinal products included in the 'List of medicinal products under additional monitoring' in force as of 22 November 2017.

**SIGNAL VALIDATION** is the process of evaluating the data supporting the detected signal in order to verify that

the available documentation contains sufficient evidence demonstrating the existence of a new potentially causal association, or a new aspect of a known association, and therefore justifies further analysis of the signal; this evaluation should take into account the strength of the evidence, the clinical relevance and the previous awareness of the association. (Fig. 5)

**RISK MANAGEMENT PLANS: GVP Module V – Risk management systems (Rev 2)- 31 March 2017:** Revision 2 is a major revision with modifications throughout and contains the following: further clarification of what RMPs should focus on in relation to an important identified or important potential risk and missing information; further guidance on the expected changes in the RMP during the life cycle of the product; updated requirements for different types of initial marketing authorisation applications, with the aim to create risk-proportionate RMPs e.g. 'abbreviated' RMPs for generic products. Revised RMP template is mandatory from 31st March 2018. Where post-authorisation safety studies and/or post-authorisation efficacy studies are a condition of the marketing authorisation, these studies are to be included in the risk management plan.

The RMP is a dynamic document that should be updated throughout the life cycle of a product. This includes the addition of safety concerns where required, but also, as the safety profile is further characterised, the removal or reclassification of safety concerns. The aim of a RMP is to document the risk management system considered necessary to identify, characterise and minimise a medicinal product's important risks. The RMP should focus on the important identified risks, important potential risks and missing information. Important identified risks are likely to have an impact on the risk-benefit balance of the product and to be included in the RMP would usually warrant (1) further evaluation as part of the pharmacovigilance plan (e.g.

to investigate frequency, severity, seriousness and outcome of this risk under normal conditions of use, which populations are particularly at risk); (2) risk minimisation activities: product information advising on specific clinical actions to be taken to minimise the risk or additional risk minimisation activities. The important potential risks to be included in the RMP are those important potential risks that, when further characterised and if confirmed, would have an impact on the risk-benefit balance of the medicinal product.

*Effectiveness of Risk Minimisation (GVP Module XVI (Rev 2):* MAH to monitor the outcome of risk minimisation measures for each medicinal product; MAH to act upon findings: update risk management system, monitor pharmacovigilance data, determine whether there are new risks and/or existing risks have changed or there are changes to the benefit-risk profile.

Evaluating the effectiveness of additional risk minimisation measures is necessary to establish whether an intervention has been effective or not, and if not why and which corrective actions are necessary. The evaluation should be performed for the additional risk minimisation tools

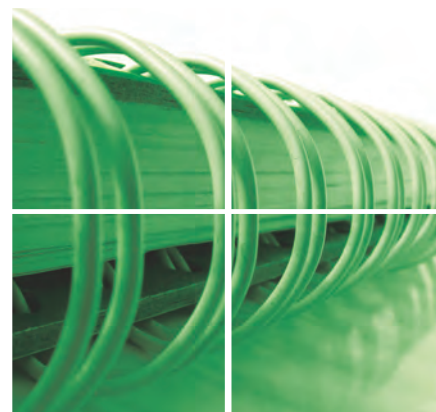
individually and for the risk minimisation programme as a whole.

*Additional monitoring GVP Module X:* Medicinal products readily identifiable by an inverted equilateral black triangle ▼ are subject to additional monitoring. The triangle will be followed by an explanatory statement in the summary of product characteristics (SmPC) as follows: “This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.”

*PBRER (PSUR) - GVP Module VII (Rev 1)* The required format and content of PSURs in the EU are based on those for the Periodic Benefit Risk Evaluation Report (PBRER) described in the ICH-E2C(R2). The PBRER format replaces the PSUR format previously described in the ICH-E2C(R1). In line with the EU legislation, the report is described as PSUR in the GVP Modules. In other words PBRER is called PSUR in the EU. The required format includes an executive summary followed by 19 sections then Appendices. PBRER is a multifunctional document with contributions from functions other than

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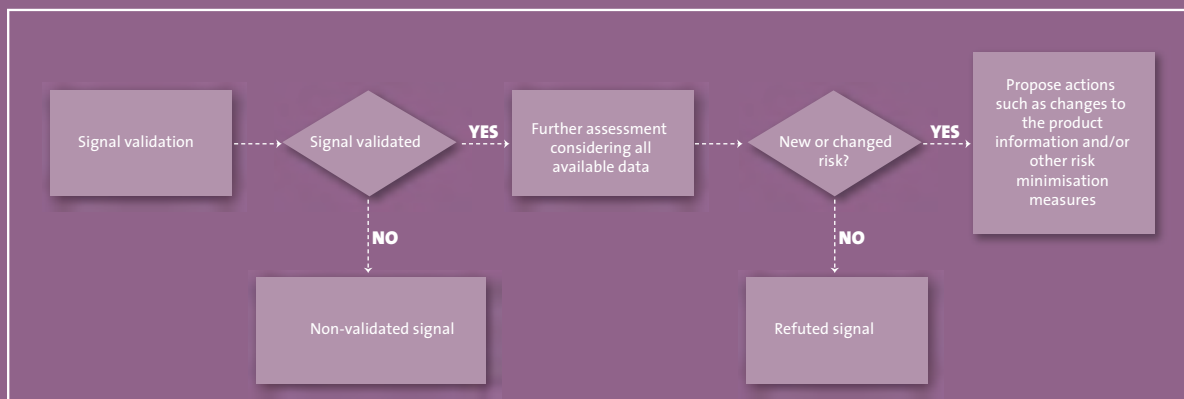


Safety.

*Pharmacovigilance System Master File - GVP Module II (Rev 2)*

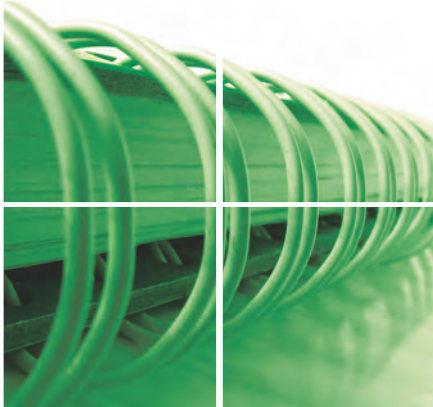
The PSMF is located either at the site in the EU where the main pharmacovigilance activities of the marketing authorisation holder are performed or at the site in the EU where the qualified person responsible for pharmacovigilance operates. It should be permanently available for

**FIGURE 5:** Possible decisions during the signal evaluation process



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inspection and provided within 7 days upon request from a competent authority. The content includes list of medicinal products (with authorisation details), EU QPPV (qualifications, responsibilities, contact details), local contact person(s), organisation structure & list of sites where various pharmacovigilance activities are undertaken, computerised system & databases, description of pharmacovigilance processes, quality system (SOPs, resource management, documentation and location of records, incl. training, audit findings), annexes.

*Safety Reporting under an IND:* describes FDA expectations for a systematic data assessment program as part of IND studies which includes the composition and role of a safety assessment committee; aggregate analyses for

comparison of adverse event rates across treatment groups (sponsors should periodically review accumulating safety data collected across multiple studies) and others.

*EU Clinical Trials Regulation:* comes into application in 2019; includes information on unblinding treatment allocation; unblinded information shall be accessible only to persons who need to be involved in the safety reporting to the Agency, to Data Safety Monitoring Boards ('DSMB'), or to persons performing ongoing safety evaluations during the clinical trial."

*BrAPP is most grateful to its speakers for their time and involvement: Prof David Linch, Dr Mike Holmes, Dr Zabid Bashir, Etta Logan and Dr Kristina Strutt*

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## PERSONAL DEVELOPMENT: Developing Resilience: Using Mindfulness At Work

*By Sharon Leighton, Sharon Leighton Consultancy Ltd in conjunction with Sue Weston, Relaxing the Mind*

LIFE IN THE workplace can be tough. Workloads increase, driving us to be obsessive about our productivity – there’s no hiding from dashboards and metrics. Many of us work in virtual teams, isolated from the social companionship of colleagues. Organisational change is a constant – new team structures, new roles, increased responsibility, and new tools.

Our job security is long gone: where we worried about the impact of outsourcing, now we feel threatened by bots and artificial intelligence. And don't get me started about the distractions of social media, emails, instant messaging or the “crack cocaine” commonly known as Candy Crush and other casual games!

So how do we cope with these everyday stresses of our modern working lives?

How can we develop emotional resilience, keep our focus and stay healthy (physically and mentally)?

Many of you would have read or heard about Mindfulness. It’s reach is ever growing. Many of your children may have learnt how to meditate at school or your employer may offer in-house or external courses. They know it has proven effects particularly on our mental health: it reduces anxiety and depression, helps improve our attentiveness and develops emotional resilience. More crudely put, less distraction and more focus = more work + less stress = less sick days and lost productivity.

But there are also misconceptions about mindfulness. It’s not about using

colouring books to take our minds off our problems, going for a walk or savoring the moment. It’s more about being mindful with what is happening right here, right now. Some of you may already be familiar with what mindfulness is and the evidence<sup>1</sup> that regularly practicing mindfulness can bring you multiple benefits in your workplace. Dr John Kabat Zinn, who brought the practice of mindfulness to the Western world, has described mindfulness as

“awareness that arises through paying attention, on purpose, in the present moment, non-judgementally. It’s about knowing what is on your mind”

In brief, mindfulness, as practiced in the West, combines 3 practices: meditation + relaxation techniques + a movement component, like yoga, T’ai Chi or qigong (which I use myself).

In this article I’ll explore the relevance of mindfulness at work in more depth and give you 5 tips you can try out today to develop emotional resilience, much needed in our busy lives. I’ve already shared my personal journey, including my initial resistance to meditation in a blog post <sup>2</sup>. Although I first used the techniques to help me cope with a painful divorce, I found collateral benefits in helping me manage my stressful workload. Running your own consultancy and training business can be a relentless slog!

### BRINGING MINDFULNESS TECHNIQUES INTO YOUR DAILY LIFE

With the long break over Christmas/New Year, you may have made resolutions for



Sharon Leighton

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### Developing Resilience:

#### Using Mindfulness At Work



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2018. Maybe you wanted to address your harmful habits (unhealthy eating, consistent late working, social media addiction, alcohol intake, etc). On a more positive note, maybe you wanted to focus on more constructive habits like more sleep, physical exercise away from your desk or having fun.

So how are they going, now we're in April?

Like throwing mud at a wall, hopefully some of it has stuck! Yet 60-80% of people cannot keep to their intentions, with complex reasons why we struggle to maintain our resolutions. Mindfulness practice includes techniques to help us examine, practice and stick to our intentions. Through practicing mindfulness, especially meditation, we train ourselves to stop and pause in the moment. We ask ourselves a few vital questions.

“How am I reacting right now? What emotions are passing through me?”

“Where am I holding these emotions in my body?”

Identifying these emotions and their embodied manifestations can help stop

us in our tracks on the path of behavioural sabotage, allowing us to alter course towards a more desired destination.

### MANAGING MEETINGS

Let's take an example to show how mindfulness is relevant at work. I'm sure attending or running meetings are a significant part of your day. Yet how many of you can truthfully say that you were *fully* present for the *whole* meeting?

By present, I mean engaged, listening with your full attention and completely clear at the end how it is relevant to you and what you need to do. I confess I've had days when I'm guilty of distracted thoughts, preoccupation with another topic or lost to daydreaming (or more likely a waking nightmare of how I'm going to meet multiple tight deadlines).

We may be feeling impatient, frustrated by long-winded discussion with no conclusion or outcomes. This impatience may have a mixture of anxiety about the “wasted” time + irritation at the inefficient meeting process + boredom at going over something you know already.



Regular meditation trains our minds to let go of our ever-present thoughts, nice or nasty, as they move through our consciousness. We learn to stand back and observe what's going on. We consider how these emotions are manifested in our bodies. This mental pause allows us to get back to a more impartial, balanced state of being: in body and mind.

Let's backtrack and take a mindful pause to re-examine that meeting situation. We can use the 2 questions above to help us recognise these feelings of impatience, irritation and frustration. We might notice that we have a tightened jaw, hunched shoulders, we're fidgeting in our chair and have a slumped posture. By pausing, we can bring our attention back to the ongoing events. In tandem, we can consciously relax our jaw, sit more upright in our chair and relax our shoulders down. Then we are ready to listen or interject, summarise the discussion so far and consider if we are ready to make a decision. By refocusing our attention, we come from the right mind state (alert but relaxed) with a powerful body posture and language of attention and equanimity. Even in a virtual meeting where no-one can see you, your emotional state and body posture will be evident in your voice.

We can use these two potent questions in many situations at work. A difficult or tedious meeting. A crucial conversation, where the stakes are high and the atmosphere charged with tension. Taking time out to pause and raise your awareness of what lies beneath is a powerful technique, essential in leadership or management roles.

### WHAT GIFT DO YOU BRING TO OTHERS THROUGH YOUR PRESENCE?

Have you ever been around someone who is predominantly negative, grumpy or picky, finding fault no matter how small? This can be very draining and unproductive, especially if you are that

person!

As the best teams have a range of personality types and a diversity of attitudes, there are always times when people can clash. How do you deal with this if you're struggling to get along with someone? Commonly known as "your opportunity to practice" to those of us who follow mindfulness!

Avoidance is one strategy but if you are in a small, close-knit team that's not realistic. Instead of expecting others to shift in their way of behaving, you can "shift" yourself! Bring an attitude of natural curiosity and compassion for others to the situation.

Aim to be impartial and use enquiry. What do you think is going on for them in their view of the world? Can you gently probe how they are viewing a situation? Many of us carry the emotional baggage of events that have happened to us in the past – those invisible scars. Learn to listen and understand more, judge less. From my own personal experience, I have found that barriers between me and people I've avoided in the past have fallen away, allowing me to see the good in them. Doesn't that sound like a quality any leader needs to cultivate?

So let's flip this argument. When you are at work (or at home), what attitude & energy do you predominantly display? What gifts do you bring to others? Self-awareness is a core competency for any aspiring professional or leader. So if you don't know, why not ask others around you who know you well – what do they value about you?

Would you like to be the person who brings balance, calm and kindness to each encounter? By practicing kindness and compassion to others, you are more likely to be viewed as a valuable team member and leader who recognises other people's talents rather than someone creating dissent and division. Through mindfulness training you can learn uncomplicated ways to access ease

## PERSONAL DEVELOPMENT: Developing Resilience:

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and balance, especially when the going gets tough. In other words, emotional resilience!

### 5 WAYS TO BE MORE MINDFUL

#### 1 BREATHE OUT

A deceptively simple and easy exercise. Often when we are tense, we breathe shallowly, from the top of our lungs. By breathing out, slowly and fully, we naturally deepen our breath which stimulates our parasympathetic nervous system. A quick and natural way to consciously relax our bodies and minds. Breathing out before you talk can give you that pause you may need to bring your attention back to the here and now.

#### 2 USE THE 2 QUESTIONS TO CHECK-IN

*What emotions am I experiencing right now?*

*How am I embodying those emotions?*

By doing a quick check-in and consciously noticing what we are feeling, it helps us realign and rebalance ourselves.

#### 3. DO A MINDFULNESS COURSE

You can't practice mindfulness by

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reading a book! Don't fall into the trap of buying books on the topic to learn more - that's like learning brain surgery from a book. You need a skilled teacher/mentor to support and guide you plus regular practice.

**4. TRY OUT A MEDITATION TASTER.**

If you'd like to try out meditation, why not listening to a guided meditation? My highly experienced meditation teacher Sue Weston has a download sound file available for your own use 3.

**5. REFRAME YOUR EXPERIENCE AND CHOOSE YOUR ATTITUDE**

Reframe your narrative of how you are experiencing life. Not so much being "swept off your feet" by events, more a case of "joyful dancing on a moving carpet".

You can choose to change your attitude to life. Do you find yourself seeing the worst, being negative, judging others or jumping to rapid conclusions? Instead you can choose to practice gratitude more often, be kind to others (without being a doormat) and be impartial. By cultivating these qualities, we become people that others want to be around, to show true leadership and live more authentic, healthy, happier lives.

Why wouldn't you want more of that?

**MORE ABOUT THE AUTHORS**  
**SHARON LEIGHTON.**

*Sharon runs a successful Medical Information consultancy; training and mentoring business helping busy managers in Medical Information achieve their goals. She is well known for presenting at conferences on globalization, quality management, organizational change and customer experience. She also teaches leadership and mentors new managers.*

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Blog: [www.sharonleighton.co.uk/news](http://www.sharonleighton.co.uk/news)  
Find her on Facebook, Pinterest, Twitter and LinkedIn

**SUE WESTON**

*Sue has been practicing and teaching mindfulness, Tai-Chi and Qigong for many years and has PG Diploma in Mindfulness Studies from Aberdeen University and Samyé College. Sue is the initiator of Relaxing The Mind activities providing Tai-Chi, Qigong and mindfulness courses locally in Monmouth and surroundings, including residential retreats over 2 weekends. She also runs a week retreat each summer on Holy Isle, Scotland. Website: [www.sueweston.com](http://www.sueweston.com)*

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**CHARISMA MASTERCLASS REVIEW**

“DO YOU LOOK in your wardrobe and decide you want to look second best today?” This comment from an image consultant was stirred when I recently attended a ‘Charisma Masterclass’ and realised that I could be bringing more of myself to my work interactions. But as with many aspects of behaviour, whilst we might know what we are aiming for, the question is how to go about achieving it.

Google charisma and you will get nearly 14 million hits; add the word ‘Research’ and you will see that they are not just from the realms of the popularist self-improvement genre, but that there is a burgeoning wealth of serious research in the applied psychology arena. This confirms the fact that sensed charisma not only predicts real-world outcomes<sup>1</sup>, but can be taught<sup>2</sup>.

A few hits down my Google search, a BBC news article, “Can you be taught to be more charismatic” featuring a London based masterclass caught my eye. The rest is history, as they say and it was not long before I had signed up myself to learn more.

Enter Richard Reid, and James Kirk, from the Pinnacle Therapy Business team, a psychologist, and actor respectively, who specialise in workplace psychology and communication.

It turns out that this sensed, yet ungraspable quality is embodied via three main qualities: Presence, Power and Warmth. It is when these are optimally titrated that the ‘magic’

happens. However, it is one thing gaining insight into what is needed, another knowing how to do it, and a further challenge developing the practical skills to actually deliver it. And we were about to explore, practice and develop each of these interwoven strands.

Having been lulled into a sense of ease by a reflective and somewhat philosophical start, reality hit with the first practical exercise. Much as I would love to share the detail of the ensuing challenge, it would be a spoiler for future attendees. Suffice to say it threw down a baseline and got us focused on the specific things we needed to do to hit that charisma sweetspot.

Being charismatic requires authenticity and personal stability through which energy can be channelled. Richard and James led us gently but firmly through some basic exercises – the scales and arpeggios of charismatic communication. We explored centring and grounding in that crucial ‘moment before’, consciously managing body language, and using short sentences for greater impact. Practical, yet remarkably powerful exercises enabled us to develop new skills whilst also providing tools for further consolidation and development. As with all new techniques they felt awkward and clunky at first, but as we got stuck in we started to realise that we were starting to get the hang of things and our confidence rose – perhaps to an extent we underestimated.

Underpinning these practical skills was a surprising amount of theory: The neurobiology and interplay of emotions



Liz Clark

## REVIEWS



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and cognition; mindfulness; unhelpful thought patterns; fixed and growth mindsets; conflict models and the role of purpose. In addition to a set of comprehensive course notes, we came away with a recommended further reading list and pointers to further material that arose from discussion. The latter reflected one of the most valuable features of Richard and James' approach - the depth of knowledge and willingness to flex and adapt to the individual needs and interests of the attendees. But what you don't get from books is the chance to try the practical elements and get bespoke input from experts. It is this practice of applied theory combined with a manageable balance of highly focused feedback that makes this course so effective.

When we re-ran the exercise on the second day, we all performed better than we had on day one. No great surprises there perhaps, given the amount of coaching we had received.

Less anticipated and pleasantly rewarding was the extent of the impact. This continued to build over the following days and weeks, igniting a virtuous circle. Colleagues commented spontaneously on warmer, more engaging communication. One even went so far as to label a presentation "inspirational"! This appeared to be a common experience for all of us who have continued to correspond, comments including: "The more time passes, the more I realise how much I enjoyed the course"; "Richard's course made me raise my eyebrows about myself"; "Last weekend switched the lights on again".

Further information on the Charisma Masterclass can be found on: <https://pinnacletherapy.co.uk/open-courses/charisma-masterclass/>

**BY DR LIZ CLARK**  
**VICE PRESIDENT MEDICAL AFFAIRS,**  
**NORGINE**

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## TRIBUTE: to Joseph Chiesa

1944 -2017

IT IS WITH great sadness that I have to report that Joseph Chiesa died suddenly on 12 September 2017. He was a partner in TranScript for a relatively short period but he was well known to and very much respected by most of us for many years, during which time he contributed hugely to pharmaceutical medicine.

He had a distinguished career working for both large and small pharmaceutical companies and CROs. He supported the design of early research for a whole range of our modern medicines. He was one of the first Fellows of the Faculty of Pharmaceutical Medicine and a Member of the Education Committee and Board of Examiners and a visiting professor at the University of Salvador (Argentina).

Joseph originally graduated from the School of Medicine at the University of Buenos Aires in 1969, receiving his Medical diploma in 1970. He received his diploma of Clinical Pharmacology in 1976 and in 1981 he achieved his Diploma of Specialist in Internal Medicine and was awarded best thesis from the Post Graduate School of the AMA for his work on "Physiological and therapeutic roles of prostaglandins". As well as having an awesome curriculum vitae, he was a wonderful person, always cheerful in the office and a real pleasure to work with. He always had time for everyone and he will be sorely missed for this and for his deeply knowledgeable and creative thinking.

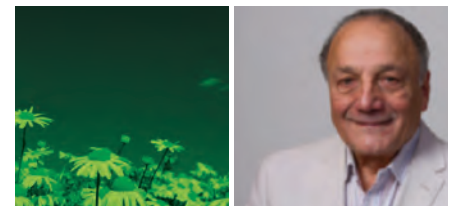
Our thoughts are with Joseph's wife and family.

*Flic Gabbay*

### DR JOSEPH CHIESA – A PERSONAL REFLECTION

I FIRST MET Joseph when I was asked to join the international division of ICI in the early 1990's. At that stage we were housed in Portakabins at the north end of the mere in Alderley Park. They were a bit rickety and leaked during heavy rain, our primitive PCs frequently falling victim to rain through the room. There were also "walkways" between the cabins and Joseph was quite an expert at the game of who can push who off and almost into the lake. He was quite nippy and a master of the blind side attack. Joseph covered Hispanic countries and I had the Middle East. Both of us were bringing "new" medicines including propofol to these markets. I had an insight here as an ex-anaesthetist, and Joseph's expertise in internal medicine and pharmacology helped with several other drugs.

Anecdotes and advice were swapped on the walkways over sandwich lunches in the summer or in the on-site pub (yes, a real pub) when it was colder. On one of the summer days I nearly did Joseph a mischief while relating a tale of misfortune from Egypt. The country manager had decided that I should visit the pyramids while en-route to see the minister of health. I was suited and booted, not really the best attire for being squashed into a narrow stone passage way. I finally got wedged and couldn't move further forward so had to retreat against the flow of humanity in the opposite direction. Filthy and with a torn shirt I emerged, while the country manager tut-tutted about me being in a poor state to meet the minister, while I tried to remind him that it was his idea to get me in there in the first place. The anecdote so amused Joseph that he



Joseph Chiesa

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## TRIBUTE:

To Joseph Chiesa



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started choking on his sandwich, requiring a quick Heimlich manoeuvre from our team leader! We used our time at Alderley Park to help the whole International group to broaden its influence in a great many countries. Occasionally we'd adjourn to the aforementioned pub at the close of the week and though he struggled manfully, Joseph never really got to like our warm flat local brew, much preferring a cold cerveza.

When I moved on to pastures new, our paths would cross at irregular intervals at BrAPP meetings, at Faculty and DIA/EMA meetings while endeavouring to keep ourselves up to date. Joseph was an enthusiast about the education of pharmaceutical physicians and we were both involved with the Faculty education committee at various times. We also were appointed to the board of examiners and both tried hard to remove the image of the board being heartless automatons trying to fail candidates. We both worked on working parties that undertook revisions of the PMST syllabus, though we don't accept blame for the sections that we weren't involved with! We worked together on BrAPP meetings and Joseph was a regular attender of the Association's education days.

When Joseph joined Covance in Leeds he sought me out to help with some of the educational activities at the site and I also became the specialty advisor for the site. We had lengthy discussions about the what/how/when of educational activities, much time was spent ensuring that maximum learning opportunities were made available. The trainees at the site benefitted from having a committed medical director who was very keen for them to develop and to document their learning and who was willing to grant time to ensure it was completed.

Joseph knew a lot of folk within this incestuous industry so when I mentioned one day that a client of mine was having a problem with cold chain

delivery, he said that he'd ask around. A few days later I was provided with a contact at a company that produced refrigerated portable containers with solar panels to provide power. My client bought a considerable number and their problem was solved, however neither Joseph nor I was ever credited with finding the solution.

We continued to work together when I acted as an independent medical monitor for some of the phase 1 studies in Leeds. Small (often biotech) clients lacked the requisite expertise to evaluate subject safety, thus I was asked to fulfil the role on their behalf. Mostly this relationship ran smoothly, but occasionally clients wanted to progress a bit further than Joseph or I deemed appropriate and some terse words were had with the clients. Joseph always prevailed, as his passion was to ensure the very highest standards of subject safety was maintained. A couple of times I was interviewed by MHRA as part of GCP audits of the Covance site and I am pleased to say that these went well, and no critical findings were observed.

Joseph was involved with IFAPP and treasured the hope that he might one day set up a formal training course for pharmaceutical physicians in Argentina and that this might be a model for much of Latin America. Sadly, the state university was not enthused, but at least one private university did want to explore this project. Despite Joseph's enthusiasm progress was painfully slow and he never realised his ambition.

Joseph's untimely death robbed his family of a fine dad and grandad, clinical pharmacology of a keen investigative mind, pharmaceutical medicine of a true professional and many people of a good and loyal friend. He is and will continue to be greatly missed.

*Dr David Blowers  
BrAPP Honorary Chairman*



## TRIBUTE: to Peter Jay MIPI, MFPM

1939-2018

*by Jane Barrett*

WE HAVE RECEIVED the sad news that Peter Jay died in February at the age of 79 after a long illness. He was known to many BrAPP members for his activities in MedicoLegal Investigations, a specialised organisation to investigate clinical trial fraud and misconduct that he set up with our own Dr Frank Wells in 1996. He was pivotal in the successful prosecution of a number of doctors found to be committing research fraud, several of them over many years. Peter was involved in training many of us in how to prevent and spot fraud, and he was always a wise and sympathetic ear to anyone concerned about the validity of their research results. His advice was clear, sound, and always relevant.

Peter's first career was with the Metropolitan Police, reaching the rank of Detective Chief Inspector, and he was the officer who arrested Dennis Nilsen, Britain's most prolific serial killer until Harold Shipman. Nilsen, also known as the Muswell Hill Killer, killed 15 young men in the late 1970s and early 1980s, and dismembered their bodies. Peter arrested him after being called by workmen who had identified human remains as the cause of a drain blockage. He kept in touch with Nilsen in custody, and Nilsen later said he was the only person who had shown him humanity. Peter was frequently interviewed and filmed in connection with the case, and as recently as 2016 appeared on television in a documentary with Trevor McDonald.

On a memorable afternoon a few years ago, Peter took the then BrAPP committee to Scotland Yard to visit the Crime Museum, where certain crime

scenes are reconstructed. He showed us a mock-up of Nilsen's kitchen, with the actual stove and large saucepan used to boil down his victims' remains. He made the story come alive; truly goose-bump producing.

But it is for his dedication to stamping out research fraud that Peter will be best remembered in our industry. This commitment was recognised by the Faculty of Pharmaceutical Medicine with Honorary Membership, an award Peter accepted with joy and humility in equal part. I was proud to nominate him for the honour, and to read his citation at the ceremony.

Peter was a wonderful friend and colleague, a wise counsel, a great supporter of those in need, and incredibly brave throughout his long-drawn out final illness. He will be much missed, and our thoughts are with his wife Linda, sons and grandchildren.



Peter Jay

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