European Federation of Statisticians in the Pharmaceutical Industry
Representing Statistical Associations in Europe

EFSPI Newsletter March 2019

In this newsletter:

Regulatory

In February, the Clinical Trials Facilitation Group (CTFG) released a Recommendation Paper on the Initiation and Conduct of Complex Clinical Trials. This document provides recommendations for sponsors regarding the authorisation and conduct of complex clinical trials. The document describes the current perspective of the Clinical Trials Facilitation and Co-Ordination Group (CTFG) on these trials and outlines the major issues that sponsors should address in the process of initiating and conducting complex clinical trials in the EU/EEA. The document highlights differences between complex clinical trials and conventional clinical trials particularly with regard to clinical trial applications (CTAs) and requests for substantial amendments. The Danish Medicines Agency who have led the authoring of the paper, are hosting a meeting on the 30th April to discuss their paper. If anyone has any comments, please contact Christine Fletcher (fletcher@amgen.com).

EMA have released their Regulatory Science Strategy to 2025 for public consultation. The five key areas include:

- Catalysing the integration of science and technology in medicine development;
- Driving collaborative evidence generation – improving the scientific quality of evaluations;
- Advancing patient-centred access to medicines in partnership with healthcare systems;
- Addressing emerging health threats;

- Enabling and leveraging research and innovation in regulatory science.

EFPIA is consolidating feedback from Industry.

In March, EFPIA launched the 'Evidence REVEAL study' exploring two prioritised key themes of 1) Use of RWE and 2) Complex Clinical Trials. Companies are being asked to share case studies of how RWE and the use of more complex clinical trials are being used to support regulatory decision making including highlighting key challenges that have been experienced to date. Survey responses are due by mid-April and a report will be issued later in 2019.

The following are new regulatory guidance documents that may be of interest:

- New draft FDA guidance on 'Rare Diseases: Natural History Studies for Drug Development'.
- Fina FDA guidance on 'Enrichment Strategies for Clinical Trials to Support Determination of Effectiveness of Human Drugs and Biological Products'

A new ICH guideline E20 will be developed on Adaptive Designs. Nominations for EFPIA representatives were provided in March and the candidates selected will be announced in a future newsletter.

The EFSPI/PSI regulatory committee are planning two webinars in the near future, so please look out for more detail on those. At our first webinar, scheduled for April 29, the topic of **Subgroups** is to be discussed. At that meeting **Aaron Dane**, **David Svensson**, and **Armin Koch** will share interesting work from the expert group on subgroups as well as reflections from a European regulatory perspective. We are also planning a webinar on reflections/implications by the **updated draft FDA guidance on adaptive designs**. **Jürgen Hummel**, **Erika Daly**, **Kaspar Rufibach**, and **Kit Roes** will give a summary of the updated draft FDA guidance, implications on confidentiality of interim results, implications on statistical software (specifically RPACT), as well as share comments from a European Regulatory perspective. This will be followed by a panel discussion by the speakers. More detail to follow.

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Scientific

A **training** on ***Early Phase Clinical Trials*** will take place in Paris on **May 20 – 22** by Prof. Thomas Jaki and Dr. Pavel Mozgunov (Lancaster University). This course presents the types of trials undertaken in early phase clinical research both in oncology and non-oncology therapeutic areas. Click here for more information, and to register click here.

Upcoming event: ***"Precision medicine in drug development".*** On **Tuesday June 4**, the joint meeting with the BBS will take place at Actelion in Allschwill (near Basel). The purpose is to bring together experts from the pharmaceutical industry, academia and the European regulatory bodies to present the current state of the art and discuss the challenges and opportunities ahead. First key speakers are announced, and a full agenda is expected early April. Click here for more information, and to register click here.

In addition, the Scientific Committee is planning for a third 1-day scientific meetings after the summer holidays. More information will follow in the coming newsletters. On March 20th , the successful meeting on Biomarkers and Subgroups took place in Gothenburg. The slides of the presentations will be made available on the EFSPI website in the coming weeks.

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Country News

APF (Germany)

The next APF Statistical Leaders meeting will take place 11.04.2019 at Boehringer Ingelheim in Ingelheim.

BBS (Switzerland)

BBS Spring Seminar: Synthetic controls – what do we need and how far can we go? May 10, 2019 from 9:00-16:30, Roche Auditorium, Viaduktstrasse, Basel. Sessions include: an overview of the use of synthetic controls, case study examples, views from regulatory, HTA and academia, and a panel discussion.

The Seminar is this year free of charge. For organizational reasons please register by sending an email in advance to fred.sorenson@xcenda.com. Registration will close by Friday, April 26, 2019

IBIG (Italy)

On the 10 May the 1st Italian Bayesian Day (for Clinical Research) will take place in Turin. This event is being hosted by IBIG in collaboration with Politecnico Turin. More details and agenda in the coming weeks.

PSI (UK)

2019 PSI CONFERENCE: 2 - 5 June, London
Data Driven Decision Making in Medical Research
There will be 2 pre-conference courses. One is on **"Stated Preference Methods: Eliciting patient preferences in the age of personalized medicine"** and is presented by members of the Benefit-Risk SIG as a follow-up and extension the popular talk they did at last year's conference. The second course is on **"Evidence Synthesis for Clinical Trials: Use of Historical Data and Extrapolation"** and will cover methods, applications and implementation using the R package RBesT". While familiarity with R is helpful, all hands-on exercises will be based on extensive example code such that SAS users are very welcome to join the course. Both courses will be very hands on and interactive and will ensure an exciting and worthwhile addition to your conference. For more details on both courses please click here and note that places on the pre-conference courses are limited.

The scientific programme is now available to view online. To view all the latest information on the Conference, please visit the PSI website.

Visit the Video-on-Demand Platform here!

FEATURED VIDEO: PSI Webinar: Avoiding Pitfalls in Supervised / Unsupervised Learning

Alexander Schacht, Andy Nicholls, Ilya Lipkovich, Jennifer Gilbride -

As the availability of big data increases and statisticians assist with predicting outcomes or understanding patterns in an ever-wider variety of scenarios then supervised and unsupervised learning methods become increasing called upon. Such machine learning algorithms offer the opportunity to understand potential predictors or clusters amongst large datasets but are also subject to the risks of overfitting or over-interpretation. The webinar video introduces ideas and shares experiences in this field. The talks introduce several supervised and unsupervised learning methods and cover data-driven subgroup identification in clinical trials, and case studies of implementation clustering algorithms.

EFFECTIVE STATISTICIAN

Communication and Data Science - 2 interesting interviews

What you can learn about communication of statistics from a statistician working for the BBC

It's surely not the norm, that a statistician from the pharma sector ends up working for BBC. But Robert Cuffe has taken this step and needs to explain statistics to non-statisticians on a daily basis. In this episode, he shares the different methods he's using. We also dive into common pitfalls that we as statisticians trap into. Finally, we also learn how we can improve our publications to make sure that the science is reported correctly in the broader news. Listen to the episode here!

Current trends in data science for pharma – findings from a qualitative survey and what we should do about it!

Do you want to learn where the health sector might be heading in terms of data science? Do you understand the opportunities and barriers in terms of the application of data science? Are you prepared to learn the individual skills needed for these changes? Then this interview with Ursula from Cytel provides you with the relevant answers! You can listen to the podcast on the homepage but also on your "podcast" app on your iPhone. If you own an android, you may use an app like Stitcher. Just search for "the effective statistician" in your app. Finally, you can also find it on Spotify.

Toxicology Special Interest Group Free Webinars

The PSI Special Interest Group "Toxicology" have a series of regular FREE webinars dealing with statistical topics faced in toxicology and related fields. The presentations will run for an hour, with approximately 45 min presentation and a Q&A session in the remaining time.

The webinars planned for 2019 are:

Tuesday 16th April 2019 - ICH S1 revision and CAD Process

Tuesday 18th June 2019 - Pig-a Assay

All take place at 14:00 UK time. Full details will be released closer to each webinar, or contact Gareth Thomas (gareth.thomas@envigo.com) to be kept up to date on all ToxSIG activities.

Webinar: MCP-Mod – Theory, Implementation and Extensions
Cytel sponsored webinar in association with PSI

Date: 8th May 2019, 14:00 - 15:30 UK time

MCP-Mod (Multiple Comparisons & Modelling) is a popular statistical methodology for model-based design and analysis of dose finding studies. This webinar will describe the theory behind MCP-Mod (plus extensions), and how to implement it within available software. Pantelis Vlachos (Cytel) will provide a brief introduction to the methodology and illustrate the MCP-MoD capabilities in EAST 6.5. Saswati Saha (University of Brehem) will discuss new variations and alternatives to MCP-Mod and show how to implement them in R. Neal Thomas (Pfizer) will present further technical details of MCP-Mod by evaluating the method using results from least squares linear model theory. Click here to register.

Estimands and Sensitivity Analysis in Clinical Trials

22nd - 23rd May 2019, Crowne Plaza, London Heathrow
Presenters: Christine Fletcher, Frank Petavy, Frank Bretz and Rob Hemmings

This two-day training course on Estimands will cover the following topics:

- Estimand Framework
- Description, strategies, and construction of estimands
- Impact on trial design, conduct, analysis and documentation
- Estimand case studies

Applications open for the 2019/2020 Introduction to Industry Training (ITIT) Course

Next course starts October 2019: The 2019/2020 course will include 3 sessions in continental Europe and 3 sessions in the UK. The course will aim to describe the drug development process, including sessions on drug discovery, toxicology, data management & role of the CRO, clinical trials, health technology assessment and marketing. For further information and to download the application form, please click here. Deadline to enrol is 30th June 2019.

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Other events

The 2019 DIA/FDA Biostatistics Industry and Regulator Forum will take place on April 8-10, 2019. Website for registration and information: https://www.diaglobal.org/en/conference-listing/meetings/2019/04/biostatistics-industry-and-regulator-forum. The *DIA/FDA Biostatistics Industry and Regulator Forum* is focused on statistical thinking to inform policy, regulation, development, and review of medical products in the context of the current scientific and regulatory environments including pharmaceuticals, biologics and biosimilars, combination products and devices, and generics. Each session will be co-chaired by an FDA/Industry team working side-by-side with today's experts to present a 360-degree perspective of statistical design, analysis, and methodological approaches to building evidence for pharmaceutical, biologic and biosimilar, combination product and device development, and approval. Now in its thirteenth year, the forum fosters open discussion of timely topics of mutual theoretical and practical interest to statisticians and clinical trialists who develop new drugs, biologics, and combination products. This unique forum advances the dialogue between industry, regulatory agencies, and academia.

The German Region of the International Biometric Society (IBS) is holding a summer school on Group sequential and adaptive clinical trial designs, 17-19 October 2019 in PfalzAkademie, Lambrecht, Germany. This summer school provides an introduction to group sequential and adaptive designs, and also covers advanced topics. The theory will be illustrated with case studies from the pharmaceutical industry. Each module of this course includes a computer practical. We will use the R software package rpact (R Package for Adaptive Clinical Trials, https://www.rpact.com/), a validated, comprehensive and freely available package for the design, simulation and analysis of group sequential and adaptive trials. More information can be found on the EFSPI website. Please register through this link.

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Job Opportunities

For information on how to submit recruitment adverts, please visit the EFSPI website: Job postings. If you are currently seeking to hire a statistician and wish to post a job advert, EFSPI are offering one free advert for every 3 adverts posted on the website.

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The World of Statistics

The World of Statistics is comprised of 2, 360 organisations across the globe. Participating organizations in The World of Statistics include national and international professional statistical societies, colleges and universities, primary and secondary schools, businesses, government statistical agencies, and research institutes. You can view the current participant and country lists involved in the World of Statistics by going to The World of Statistics website http://www.worldofstatistics.org/.

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Chrissie Fletcher
EFSPI Communications Officer