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

EFSPI Newsletter February 2014

In this newsletter:

Regulatory Update

Draft guideline on the investigation of subgroups in confirmatory clinical trials

EMA have published a draft guideline on the investigation of subgroups in confirmatory clinical trials (see http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/02/WC500160523.pdf). The deadline for comments is July 31st 2014.

The EFSPI/PSI Regulatory Committee will be submitting consolidated comments. At present, we intend to organize a meeting in April or May in London to discuss this guideline. We will update you as soon as we can on the date and also of the deadline by which we need your comments. We would of course like to have your comments before the workshop. Alan Phillips (Alan.Phillips@iconplc.com) kindly volunteered to take the lead for this guideline. Please email Alan if you would like to get involved in the commenting process.

When commenting **please use** the official template (see http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500004016). This makes collating and consolidating them much easier. Thanks!

Qualification opinion on new statistical methodology

CHMP has adopted a qualification opinion and concluded that the "MCP-Mod" (multiple comparison procedure - modelling) approach can be qualified as an efficient statistical methodology for model-based design and analysis of phase II dose finding studies under model uncertainty. The MCP-Mod approach is efficient in the sense that it uses the available data better than traditional pairwise comparisons. It is noted that a number of alternative approaches might be considered, of which

MCP-Mod is only one. This qualification opinion does not seek to compare between these alternative approaches. For further information see:

- Qualification opinion of MCP-Mod as an efficient statistical methodology for model-based design and analysis of phase-II dose-finding studies under model uncertainty
  Annexes:
  Applicant submission:Request for CHMP Qualification Opinion - Annex 1 (initial request, Novartis)

Applicant submission:Request for CHMP qualification opinion response to questions dated 11 June 2013 - Annex 2 (response)
Applicant submission:Discussion meeting for MCP-Mod qualification opinion request - Annex 3 (Novartis presentation)

Overview of comments on the qualification opinion of MCP-Mod as an efficient statistical methodology for model-based design and analysis of Phase II dose finding studies under model uncertainty'

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Special Interest Group (SIG) News

This year all current eight SIGs (Special Interest Groups) will present themselves in the EFSPI Newsletter. Each SIG will tell you more about their key interests, goals and objectives, achievements, deliverables, and how you can contribute. We start in February with the Health Technology Assessment (HTA) SIG (see below) and then followed by the Biomarkers, Medical Devices, Toxicology, Epidemiology & Safety, Integrated Data Analysis, Benefit/Risk, and finally Modelling & Simulation SIGs.

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SIG of the month: Health Technology Assessment (HTA)

The HTA SIG was formed at the beginning of 2010 and it was set up to provide statisticians working in the Pharmaceutical Industry engaged in Health Technology Assessments across Europe, and others in related fields of research, an opportunity to:

- Collaborate and discuss strategies and methodology being applied in this area of research;
- Exchange information and share case studies and statistical/analytical challenges faced in HTA research;
- Keep abreast of new research and methodological developments;
- Promote and highlight opportunities for statisticians to make a positive impact in HTAs
- Interact with key opinion leaders in HTA research;
- Organise and/or participate in workshops related to HTAs.

As of February 2014, the HTA SIG has approximately 20 individuals actively participating in the SIG. Members represent 15 companies (including a few independent consultants) who are located in a variety of European countries (UK, Switzerland, Germany, The Netherlands, France and Denmark)

with a couple of colleagues based in the USA. The HTA SIG meets on a quarterly basis for a 3 hour meeting via teleconference.

Over the last 3 plus years, the SIG have written an HTA handbook which provides an introduction to HTA for statistical colleagues new to HTA. It has organised a number of sessions at conferences and scientific meetings relating to HTA topics sponsored by PSI, EFSPI and the International Society of Pharmacoeconomics and Outcomes Research (ISPOR). Examples include discussing the statistical challenges in HTA, holding a mock HTA committee meeting; and leading a debate on how to integrate reimbursement needs in drug development). The SIG have written a number of manuscripts submitted and/or published to Pharmaceutical Statistics including a paper on network meta-analysis, papers on subgroup analyses to support clinical effectiveness and cost-effectiveness for an HTA, a paper on adjusting overall survival for treatment switches, and a paper on statistical perspectives of utility values in HTA. The SIG will continue to research and promote methodologies important for HTA. The SIG have held numerous virtual round table discussions with key experts in the field of HTA including statisticians who have specialised in HTA and health economics, representatives from ISPOR, and representatives from the EFPIA HTA Taskforce. Within the SIG meetings, we've shared HTA case studies and collaborated with health economic colleagues in improving our understanding of HTA.

Anyone interested in seeking further information on the HTA SIG and/or has any questions or feedback please contact Chrissie Fletcher (Chair, fletcher@amgen.com)

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5th EFSPI Statistical Leaders Meeting

Already the 5th EU Statistical Leaders Meeting will this year be held Wednesday June 11 in Basel hosted by Roche. Key topics will be to follow up on Clinical Trial Data Sharing, information exchanges with the new "Integrated Data Analysis" SIG and the "Pharmaco-Epidemiology" SIG. Furthermore, the meeting will discuss the many new developments involving different trial designs and different sources of data such as EMAs PAES (Post Approval Efficacy Studies), EFPIAs new Clinical Trial Design Task Force as part of the revamping of the R&D model, and EMAs initiative of parallel advice with both regulators and HTA bodies. Clearly there is significant change within the Pharmaceutical Industry and the Stats Leaders Forum will ensure the EU statistical community is informed of the changes and the potential impact to us, and seek opportunities for EFSPI and all statisticians in Europe to shape the strategy forwards. This year's Organizing Committee consists of Hans-Ulrich Burger, Chrissie Fletcher, Byron Jones, George Quartey, and Stefan Driessen. For more information about this meeting, or any other comments/question on this Forum, please contact Stefan Driessen **(stefan.driessen@abbott.com).**

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Scientific Update

EFSPI is planning to organise three scientific meetings in 2014. A joint meeting with PSI on the new subgroup guideline is planned in April or May in London (more information on this topic can be found in the regulatory update section above). Proposed topics for the other two meetings are

Health Technology Assessment and Modelling approached like the MCP-Mod approach (see discussion above).

EFSPI / PSI is partner in the FP7 project called ASTERIX, which focuses on the development of more efficient and effective research designs to study new drugs and treatments for rare diseases. Together with two other FP7 projects (IDEAL and InSPiRe) ASTERIX will organise a symposium on small population on 1st and 2nd of July in Vienna. For more information visit http://statistics.msi.meduniwien.ac.at/hp/small2014/

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The World of Statistics update

The new website for The World of Statistics which is a follow on to the International Year of Statistics (Statistics 2013) is up and running, please be sure you have the new website booked marked as a favourite. The World of Statistics currently has a total of 2,353 participating organizations from a whopping 129 countries. As a reminder, the objectives of the World of Statistics are:

- Increasing public awareness of the power and impact of statistics on all aspects of society
- Nurturing statistics as a profession, especially among young people
- Promoting creativity and development in the sciences of probability and statistics

The International Prize in Statistics Foundation, an organization committed to developing an annual "Nobel-like" prize in statistical science, is now established. This new prize will greatly increase media and public awareness of the growing importance of statistics to modern life and promote understanding of the myriad and diverse ways that statistical science is impacting the well-being of billions of people. You can learn more about the International Prize in Statistics, which is in the early stages of development, by visiting statprize.org.

Do visit the World of Statistics website to check out latest news and see what is going on in all fields of statistics around the world.

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And finally…..

If you are currently seeking to hire a statistician and wish to post a job advert, see the "Advertisements" area on the EFSPI website at www.efspi.org and view the "Job Postings" for instructions. EFSPI are offering one free advert for every 3 adverts posted on the website.

To add your e-mail address to the EFSPI mailing list, click on "Sign up to our newsletter" on the homepage of the EFSPI website.

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