European Federation of Statisticians in the Pharmaceutical Industry

Representing Statistical Associations in Europe

EFSPI Annual Report 2017

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Highlights from the EFSPI President & Vice President

EFSPI had a very successful 2017. A new membership structure was introduced where the membership fees are based on different sizes of local associations.

The regulatory committee were busy reviewing a variety of draft guidelines and supporting two expert working groups in confidentiality of interim results and subgroup analyses.

Three scientific meetings were held on topics including statistical aspects of safety data in clinical trials, oncology and survival analysis, and latest trends in Health Technology Assessment (HTA). A webinar was also held on Integrated Data Analysis.

EFSPI held its second annual Regulatory Statistics Workshop which was well attended and had an increased number of delegates compared to 2016. Key topics of discussion included XXX.

The EFSPI Statistics Leaders meeting continues to be well attended with the focus this year including statistical decision making, interactions with academia, patented trial design, data science and latest updates from the Special Interest Groups.

Marisa Bacchi (Switzerland)
President

Uli Berger (Switzerland)
Vice-President

Finance

In 2017 the membership structure was restructured, and new membership fees introduced where the fee level is based on the size of the local association. The total income received remains the same.

EFSPI revenues and profits were significantly increased by the EFSPI Regulatory Statistics Workshop, the second time the meeting was run, with an increase in the number of delegates attending compared to 2016. There was reduced income from scientific meetings as 2 meetings were held rather than 3. Expenses continue to be closely monitored.

EFSPI Income and Expenses 2017

	Actual €	**Budget €**	Variance €
Income			
Membership Fees	12.250	12.250	0
Scientific Meetings	11.770	18.000	(6.230)
EFSPI Statistics Leaders Meeting	7.740	6.000	1.740
EFSPI Regulatory Statistics Workshop	41.295	33.000	8.295
Recruitment Web Advertisement	2.450	1.400	1.050
	77.514	70.650	6.864
Expenses			
Executive Office Hours	13.412	14.820	1.408
Attending Meetings	0	450	450
Web Development & Hosting	1.261	930	(331)
Office Costs	874	1.200	326
Bank Charges	1.079	2.000	921
Scientific Meetings	9.550	10.000	(450)
EFSPI Statistics Leaders Meeting	1.238	2.000	762
EFSPI Regulatory Statistics Workshop	21.376	23.000	1.624
EFSPI Incorporation	0	1.500	1.500
Anticipated revenue sharing		1.000	(1.000)
	47.512	55.900	8.388
Net result for the year	30.002	14.750	15.252

Balance

	2017 €	2016 €
Current assets		
Debtors	9.185	4.445
Sundry debtors	239	239
Prepayments	72	144
Accrued Income	13.895	-
Bank - €	84.502	68.558
Bank - £ (Converted to €)	5.588	1.021
	113.481	74.407
Current liabilities		
Creditors	10.006	830
Accruals	3.262	3.365
	13.268	4.195
Revenue reserves		
Balance brought forward	70.211	41.767
Result for year to date	30.002	28.444
	100.213	70.211

Birgitte Biilmann Rønn (Denmark)

EFSPI Treasurer

EFSPI Regulatory Statistics Workshop



The 2nd EFSPI regulatory statistics workshop took place on the 5th-6th October 2017 in Basal, Switzerland. Approximately 200 industry, regulatory, and academics registered for the workshop, including clinicians who attended the first day and the session on estimands.

The topics discussed at the workshop included the draft FDA guideline on multiple endpoints, estimands with case study presentations, role of early development in regulatory approval, predictive biomarkers for therapeutic decision making and disease specific drug development issues. There was also a session allowing individuals from the audience to present on short topics followed by a panel discussion.

The materials from the workshop are stored on the website (www.efspi.org).

Hans Ulrich Berger Egbert Biesheuvel Christoph Gerlinger

Members of the EFSPI Regulatory Statistics Workshop planning team

Regulatory Affairs

Objectives

The role of the regulatory committee is to provide the EFSPI/PSI viewpoint on regulatory issues. This includes promoting best practice, reviewing regulatory policy and guidelines, driving debate on future guidance, and engaging with statisticians in European regulatory agencies.

General

During 2017 the regulatory committee held six regular committee meetings, as well as meetings with the EMA's Biostatistics Working Party (BSWP) and the MHRA statisticians. The committee coordinated the review of several regulatory guidance documents (more detail below). Committee members have contributed to EMA and industry workshops, as well as webinars, on topics such as estimands, first-in-human trials, and clinical trial transparency and anonymization. In addition; members of the committee helped organize the 2nd EFSPI workshop on regulatory statistics held in Basel as well as the regulatory hot topic session at the PSI conference in London.

In June the chair of the regulatory committee transferred to Christoph Gerlinger from Anna Berglind, who is now the Co-Chair of the committee.

Expert Groups

Two regulatory expert working groups have been active during 2017: the expert group on confidentiality of interim results was established following the 2016 meeting with the BSWP. This group has authored recommendations that were shared with the BSWP in 2017, and that will be shared further via a position paper. In addition, the expert group on subgroups continued the work on developing a best practice for subgroup analysis and is currently finalizing a paper on the topic to be submitted to Pharmaceutical Statistics.

Meetings with statisticians from regulatory agencies

The EFSPI/PSI regulatory committee met with the EMA's BSWP on October 27, 2017. Topics discussed included: confidentiality of interim results, non-proportional hazards as it relates to time to event endpoints, real world evidence in rare diseases, statistical assessment of quality attributes, and innovation in clinical trial design.

On November 20, 2017, the regulatory committee met with the MHRA statisticians in London. Topics discussed included: umbrella and basket trials, inconsistencies between hypothesis tests and estimates, statistical assessment of quality attributes, estimands, pragmatic clinical trials and the use of real-world evidence/data generated in clinical practice in regulatory decision making, risk-based monitoring, and Bayesian methods for incorporating historical data into paediatric trials.

Guidelines

The regulatory committee collated comments on the following documents during the year:

- EMA's draft Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/07/WC500232186.pdf)
- FDA´s draft guidance on Multiple Endpoints in Clinical Trials Guidance for Industry (https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm536750.pdf)
- EMA's draft guideline on multiplicity issues in clinical trials (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/03/WC500224998.pdf)
- EMA's draft reflection paper on statistical methodology for the comparative assessment of quality attributes in drug development (EMA) (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/03/WC500224995.pdf)
- The draft ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to guideline on statistical principles for clinical trials (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/08/WC500233916.pdf)
- EMA's draft reflection paper on the use of extrapolation in the development of medicines for paediatrics (Deadline in 2018) (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/10/WC500236640.pdf)

Special thanks to Bruno Boulanger, Maylis Coste, Erika Daly, Christoph Gerlinger and Alan Phillips for collating comments for the committee.

Also, special thanks to Anna Berglind for compiling the annual report.

Christoph Gerlinger (Germany)

Regulatory Chair

Scientific Affairs

The Scientific Committee organised three successful 1-day scientific events in Europe in 2017:

1. The 1st one was a joined EFSPI / PSDM event on '**Statistical Aspects of Safety Data in Clinical Trials**', in the Netherlands on 23rd of June hosted by Astellas. This meeting focused on three areas, analyses of Adverse Events, Data Monitoring Committees and presentation of safety data. With more than 60 participants, lively presentations and interactive discussions it was a successful meeting. The presentations can be found here https://www.efspi.org/EFSPI/Events/Archive_Items/European_Statistical_Meeting_on_Analysis_of_Safety_Data.aspx
2. The 2nd 1-day meeting on '**Oncology and Survival Analyses**' took place on 17th of November at BMS in Brussels. This meeting discussed recent advances in survival analysis methods. Although less than 60 attendees, the scientific contents were very good and two regulators (from Sweden and the Netherlands) participated. The presentations can be found here https://www.efspi.org/EFSPI/Events/Archive_Items/European_Statistical_Meeting_Oncology_and_Survival_Analysis.aspx
3. The 3rd one was a joined EFSPI/PSI meeting on '**Latest Trends in HTA**', which took place on 28th of November hosted by MSD in London. This meeting provided an update on latest trends in HTA including the Real-World Evidence Navigator tool created by the IMI GetReal Project, as well as the involvement of patients in HTA. Almost 50 people attended, not only statisticians. Presentations can be found on the PSI website https://www.psiweb.org/events/event-item/2017/11/28/default-calendar/european-statistical-meeting-latest-trends-in-health-technology-assessments

In addition, a webinar on '**Spotlight on the Integrated Data Analysis**' was organised on 28th of September. This webinar reprised the three presentations given during the special session at the PSI annual conference devoted to the IDA Special Interest Group, the common theme between them was that they all dealt with either collecting, reporting or analysing safety data.

In 2017, Carl-Fredrik Burman (Astra Zeneca, Sweden) stepped down from the committee and David joined us. As a result the Scientific Committee consisted of the following members:

- Francois Aubin (Venn Life Sciences, France)
- Egbert Biesheuvel (Nutricia Research, Netherlands) - Chair
- Alexandra Green (Takeda, UK) – pregnancy leave

- Axel Krebs-Brown (Astellas, the Netherlands)
- Emmanuel Quinaux (IDDI, Belgium)
- Pierre Verweij (Idorsia, Switzerland)
- David Wright (Astra Zeneca, UK)

Julie Mellish (KSAM, UK) – Administration

Egbert Biesheuvel (the Netherlands)

Scientific Chair

Statistics Leaders Meeting

In 2017 the Statistics Leaders Forum consisted of about 50 active members from all EFSPI countries and from a wide range of EU pharmaceutical companies, or affiliates of ex-EU companies.

This year 39 people from 10 different countries representing 31 different pharmaceutical companies and CROs attended the 2017 EFSPI Statistical Leaders Meeting, held in Ludwigshafen, Germany, on July 4, kindly hosted by AbbVie. The 8th meeting saw a row record number of participants and companies. Topics on the agenda were: Statistics in Decision making, Interaction with Academia, Patented trial designs, and Data Science.

The purpose of the EFSPI Statistics Leaders meeting is to bring together leaders and managers in statistics groups from the EU pharmaceutical industry to network and discuss strategies to help EFSPI set its strategic objectives for the future.

After kind welcome to all participants by Stefan Driessen, Chair of the Statistical Leaders forum, the first session on **Statistical Decision making**, a follow-up on last year's meeting, was presented by Maylis Coste and Sylvain Nicholas. Several use cases were presented and discussed. The discussion in the group showed consensus that this topic is of strategic importance and that possibly a new SIG might drive this best by sharing business cases and methodological support.

Next Hans-Ulrich Burger kicked of an interactive discussion on the status and desired strategic direction of the **Interaction with Academia**. Several questions were put to the group (Do we want closer relationship? Do we know what "they" want?, etc.). From the discussions as key message emerged that deeper interaction is important if we want to be

successful. Also we may have to put more effort in understanding the needs from Academia and a working group out of EFSPI might be a good approach (similar to the group on interaction with Regulators).

A new item in the meeting is that the host, this year AbbVie, is invited to bring up a topic of their interest. Daniele Compagnone, AbbVie, introduced the interesting topic of **Patented Trial Design**, that is study designs that have been patented. One specific example was given (patent existing in US) and discussed in-depth. The Forum deemed such barriers to the use of trial design problematic and against the principle of scientific freedom. However, as no other examples are known, the one discussed may remain an "outlier".

The afternoon was largely spent on the by now traditional interactive workshop in this meeting on a special topic. This year it was **Data Science**. Data Science is an emerging, multi-functional area, that is on many people's radar (in academia, companies, governments) with the ongoing digitalization. An excellent introduction to the topic was given by James Weatherall together with Andy Garrett. Also the results of an internal Statistical Leaders Forum survey were presented indicating the level of engagement by the group in this area, which showed clear variability in the maturity and number of activities in Data Science. Nevertheless, a general trend was shared to see the science further mature with upcoming focus and work in areas as Big Data, and IoT (Internet of Things). The four break-out groups came back with numerous ideas on how to proceed in the area and their role in it (see summary on our website, including link to 'get started" paper by the RSS Data Science section). The general consensus was that Data Science is an area to stay and that statisticians and EFSPI should embrace it and by engaging promoting statistical rigor rather than rigidity. Definitely a topic that will need follow-up by the Statistical Leaders group.

The meeting was closed with discussing EFSPI's priorities for the coming years. The directions of the last years with more outgoing communication and interaction were re-emphasized (regulators, academia, health organizations) and focus areas such as Data Science were brought up to form part of the strategic direction of EFSPI.

All material from the EU Statistics Leaders Meetings is available on the EFSPI website:

https://www.efspi.org/

Stefan Driessen (The Netherlands)

Statistics Leader Forum Chair

Special Interest Groups

A summary of all the SIGs active in 2017 is provided below:

Biomarker (leader = Athula Herath, heratha@MedImmune.com)

Benefit-risk (leader = Alexander Schacht, schacht_alexander@lilly.com)

Health Technology Assessment, HTA (leader = Chrissie Fletcher, fletcher@amgen.com)

Integrated Data Analysis (leader = Byron Jones, byron.jones@novartis.com)

Medical Devices (leader = Martin Wadepuhl, wadepuhl.m.vsa@t-online.de)

Modelling & Simulation (leader = Chris Campbell, ccampbell@mango-solutions.com)

Real World data (leader = Maurille, maurille@amgen.com)

Toxicology (leader = Gareth Thomas, ThomasG@UKOrg.Huntingdon.com)

Small Populations (leader = Egbert Biesheuvel, egbert.biesheuvel@danone.com)

AIMS (leader = Craig McIlloney, craig.mcilloney@ppdi.com)

Stefan Driessen (the Netherlands)

Special Interest Group Chair

Communications

Monthly newsletters were distributed in 2017. Key highlights announced during the year included news from the Special Interest Groups, upcoming events, World of Statistics latest news, and celebrating milestones such as World Statistics Day and Clinical Trials Day. All newsletters are available on the EFSPI website (www.efspi.org).

Chrissie Fletcher (UK)
Communication Officer

Operations Board Summary

The Operations Board had monthly teleconference meetings over the year, during which all ongoing and future activities were reviewed and issues discussed.

The board is composed of: Marisa Bacchi (President), Hans Ulrich Burger (Vice-President), Birgitte Biilmann Rønn (Treasurer), Egbert Biesheuvel (Scientific Affairs), Stefan Driessen (Statistical Leaders Meeting and SIGs), Chrissie Fletcher (Communications Officer), Christoph Gerlinger (Regulatory Affairs), and Julie Mellish (Executive Office).

Council Membership

In 2017, 10 countries national associations of pharmaceutical statisticians from 10 European countries were represented within EFSPI, totalising a combined membership of more than 2200.

Members of the EFPSI Council at the end of 2017 are listed in the Appendix.

Council Summary

Two Council meetings were held in 2017. In addition to the two face to face meetings, two web conferences were held.

Executive Office

The Executive Office facility continues to be provided by Kingston Smith (UK). Julie Mellish is the Secretariat for EFSPI.

Appendix: Council members at the end of 2017

Belgium
Emmanuel Quinnaux, IDDI
An Vandenbosch, Janssen

Denmark
Mette Krog Josiassen, Lundbeck
Birgitte Biilmann Rønn, Novo Nordisk

Finland
Sami Virtanen, Orion Pharma
Teppo Huttunen, 4Pharma

France
Emmanuel Pham, Ispen
Maylis Coste, Servier

Germany
Justine Rochon, Boehringer Ingelheim
Christoph Gerlinger, Bayer

Italy
Fabio Montanaro, Latis
Marco Costantini, GSK

Netherlands
Stefan Driessen, Abbott
Egbert Biesheuvel, MSD

Sweden
Mattis Gottlow, AstraZeneca
Magnus Kjaer, AstraZeneca

Switzerland
Hans Ulrich Burger, Hoffmann-La Roche
Marisa Bacchi, Idorsia

UK
Chrissie Fletcher, Amgen
Rebecca Sudlow, Roche