European Federation of Statisticians in the Pharmaceutical Industry

Representing Statistical Associations in Europe

EFSPI Annual Report 2016

Date: September 2019

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Highlights from the EFSPI President & Vice President

EFSPI had a very successful 2016. EFSPI held its first annual Regulatory Statistics Workshop which was well attended. A large number of regulatory statisticians from Europe were able to attend and present in sessions alongside Industry and academic representatives. The workshop was the primary driver for EFSPI achieving record breaking profits and increased revenues compared to previous years. This additional revenue has enabled the EFSPI reserves to be at a more acceptable level reducing financial risks for EFSPI. In addition, some of the additional funds will be re-invested in EFSPI in 2017 and beyond, enabling EFSPI to increase and broaden its activities and support to the local associations and EU statistical community.

Two scientific meetings were held on topics including biomarkers and subgroups and evidence synthesis. A webinar with the modelling and simulation Special Interest Group (SIG) promoted best practices for the increasing use of modelling and simulation supporting drug development.

The EFSPI Statistics Leaders meeting continues to be well attended with the focus this year including precision medicine and biomarkers, key updates form the SIGs, and an interactive debate on the future of R&D and key skills statisticians need to maximise their success and professional careers.

Marisa Bacchi (Switzerland)
President

Chrissie Fletcher (UK)
Vice-President

Finance

In 2016 EFSPI revenues and profits were significantly increased by the first EFSPI Regulatory Statistics Workshop which was a huge success and where a large number of delegates attended. In 2015 it was challenging to predict both the income and expenses supporting this new workshop, however the delegate fees were purposely kept as low as possible to increase the number of delegates registering, and the costs were also carefully managed to minimise the risks to EFSPI. EFSPI reserves were increased ~ 70% primarily due to the additional profit generated from the EFSPI Regulatory Statistics Workshop.

EFSPI Income and Expenses 2016

	Actual €	**Budget €**	Variance €
Income			
Membership Fees	12.514	12.514	0
Scientific Meetings	19.256	18.000	1.256
EFSPI Statistics Leaders Meeting	6.240	5.000	1.240
EFSPI Regulatory Statistics Workshop	32.231	9.000	23.231
Recruitment Web Advertisement	3.150	1.050	2.100
	73.371	45.564	27.827
Expenses			
Executive Office Hours	14.592	14.820	228
Attending Meetings	0	650	650
Web Development & Hosting	963	1.795	832
Office Costs	1.251	1.140	(111)
Bank Charges	601	2.250	1.649
Scientific Meetings	13.240	12.000	(1.240)
EFSPI Statistics Leaders Meeting	1.261	2.000	739
EFSPI Regulatory Statistics Workshop	13.039	6.000	(7.039)
EFSPI Incorporation	0	1.500	1.500
	44.947	42.155	(2.792)
Net result for the year	28.444	3.409	25.035

Balance

	2016 €	2015 €
Current assets		
Debtors	4.445	1.142
Sundry debtors	239	
Prepayments	144	383
Accrued Income	-	5.190
Bank - €	68.558	39.122
Bank - £ (Converted to €)	1.021	3.225
	74.407	49.062
Current liabilities		
Creditors	830	2.015
Accruals	3.365	5.280
	4.195	7.295
Revenue reserves		
Balance brought forward	41.767	39.322
Result for year to date	28.444	2.446
	70.211	41.767

Birgitte Biilmann Rønn (Denmark)

EFSPI Treasurer

EFSPI Regulatory Statistics Workshop



The 1st EFSPI Regulatory Statistics Workshop took place on *September 12th and 13th* 2016 in Basel, Switzerland. Approximately 160 delegates attended the workshop, including representatives from Industry, academic and regulatory agencies. The meeting was a huge success.

The key themes and topics covered in the workshop included: estimands; extrapolation; benefit-risk assessments; and statistics in quality attributes. 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 purpose 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

2016 has been another exciting year for the Regulatory Committee. During the year the committee held seven regular committee meetings, held meetings with the EMA's Biostatistics Working Party and the MHRA statisticians in London, and led the review of several regulatory guidance documents (more detail below). The Regulatory expert group on Subgroups continued the work on developing a best practice for subgroup analysis and held a training event on subgroups at the PSI conference in Berlin May 2016. The group is currently finalizing a paper on the topic to be submitted to Pharmaceutical Statistics.

In June 2016 the chair of the Regulatory Committee transferred to Anna Berglind from Christoph Gerlinger. Christoph, who is the EFSPI regulatory chair, is now the Co-Chair of the committee, taking over that role from Lesley France. In addition, committee members have contributed to EMA and industry workshops on extrapolation, Clinical Trial Transparency and anonymization; estimands, as well as the successful 1st EFSPI Workshop on Regulatory Statistics held in Basel in September 2016.

Meetings with statisticians from regulatory agencies

The EFSPI/PSI regulatory committee met with the EMA's BioStatistics Working Party (BSWP) on September 30, 2016. Topics discussed included: guideline on multiplicity Issues in clinical trials; statistical methodology for the comparative assessment of quality attributes in drug development; control of Type I error in bioequivalence studies, treatment switching in oncology; guidance on data monitoring committees; confidentiality of interim results; role of non-randomized data in regulatory decision making; and estimands.

On the 23rd November 2016 the Regulatory Committee met with the MHRA statisticians in London. Topics discussed included: estimands; real world data; EMA publication of trial data; first in human studies; confidentiality of interim results; use of R and other specialist

software; single arm trials for drug approval; parametric survival curve modelling; evaluation of safety and quantitative benefit-risk in drug development; and the role of statisticians and quantitative methods in drug development decision making.

One of the outcomes of these meetings is that the Regulatory Committee is initiating a workgroup on the topic of Confidentiality of interim results.

Guidelines

The regulatory committee commented on the following documents during the year:

- EMA's "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/2016/11/WC500216158.pdf). Special thanks to Maylis Coste and Bruno Boulanger who are leading this work.
- EMA's release of the draft "ICH guideline E17 on general principles for planning and design of multi-regional clinical trials" (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/07/WC500211312.pdf). Special thanks to Aaron Dane who took the lead.
- EMA's draft "Guideline on evaluation of anticancer medicinal products in man" (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/03/WC500203320.pdf. Special thanks to Tony Sabin who took the lead.
- ICMJE's data sharing proposal, editorial in New England Journal in Medicine): "Sharing Clinical Trial Data — A Proposal from the International Committee of Medical Journal Editors", which would require authors to make available de-identified individual patient-level data (IPD) underlying clinical trial results included in a manuscript no later than 6 months after the release of the publication, and a data sharing plan to be included in registering a clinical trial.

Special thanks to Anna Berglind for compiling the annual report.

Christoph Gerlinger (Germany)

Regulatory Chair

Scientific Affairs

The Scientific Committee organised two successful 1-day scientific events in Europe in 2016:

1. The 1st one on '**Biomarkers and Subgroups**' was held on the 24th June in Leiden, the Netherlands hosted by Astellas. It was well attended by more than 50 attendees. A lively and interactive panel discussion concluded a successful meeting. The presentations together with the agenda and a summary of this day are available on the EFSPI website https://www.efspi.org/EFSPI/Events/Archive_Items/Biomarkers_and_Subgroups.aspx

2. The other 1-day scientific event on '**Evidence Synthesis**' took place on the 22nd of November in Brussels (hosted by BMS). This meeting discussed methodological considerations relating to synthesizing evidence to support drug development and market access activities. It was a successful meeting with a variety of presentations and an interactive panel discussion at the end of the meeting. Presentations of the meeting are available on our website https://www.efspi.org/EFSPI/Events/Archive_Items/European_Statistical_Meeting_on_Evidence_Synthesis.aspx

Together with the Special Interest Group on M&S, we organised a webinar on '**Best Practice in Modelling and Simulation**' on October 4th. This webinar covered recent proposed Best Practice for M&S which has been accepted for publication in Pharmaceutical Statistics. Speakers will discuss how M&S can be integrated into the drug development process from discovery to post-marketing, and how M&S practitioners can keep to the appropriate best practice, when applications and impact of M&S vary so much. These presentations are based on the presentations given at the PSI conference in Berlin in May 2016 and include new material.
https://www.efspi.org/EFSPI/Events/Archive_Items/Best_Practice_in_Modelling_and_Simulation.aspx

In 2016, the Scientific Committee consisted of the following members:

- Francois Aubin (Venn Life Sciences, France)
- Egbert Biesheuvel (Nutricia Research, Netherlands) - Chair
- Carl-Fredrik Burman (Astra Zeneca, Sweden)
- Alexandra Green (Takeda, UK)
- James Matcham (AstraZeneca, UK)
- Axel Krebs-Brown (Astellas, the Netherlands)
- Emmanuel Quinaux (IDDI, Belgium)

- Pierre Verweij (Idorsia, Switzerland)
- Julie Mellish (KSAM, UK) – Administration

Egbert Biesheuvel (the Netherlands)

Scientific Chair

Statistics Leaders Meeting

In 2016 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 34 people from 8 different countries representing 29 different pharmaceutical companies and CROs attended the 2016 EFSPI Statistical Leaders Meeting. This is a record number of participants and companies in this 7th meeting in a row, this year held in Paris on July 5, kindly hosted by Sanofi.

The first session on regulatory and public interactions made clear that there is broad EU participation in the regulatory committee and engagement in key regulatory forums with working groups in place on topics as data transparency, estimands, and statistics in quality. Further there are good links with EFPIA. One message from the group was that in the near future more attention should also be given to the communication on consortiums as IMI. In this year's meeting three SIGs were presenting. The relatively new SIG Small Populations has kicked off with still small but active group and expressed that more members can join and a need for case studies. The SIG Modelling & Simulation updated the group on the release of their Best Practice guidance published in Pharmaceutical Statistics and the SIG will hold a seminar on it. The group was very much invited to use it and give the SIG feedback. The new SIG AIMS (Application and Implementation of Methodologies in Statistics) presented its charter and through a questionnaire of 25 possible topics queried the Stats Leaders group for prioritization and got very helpful feedback to further steer their activities. Especially, the validation of R and graphical application was deemed of high interest.

An interesting discussion was on the topic of Precision Medicine and Biomarkers. How this is supported very much differs between companies (by special expert groups, by early development statisticians, or typical phase2/3 statistician). Not so many success stories are available and that hampers further resourcing this area. Another item mentioned was that collaboration is needed and statisticians with biomarker expertise but also generalists with regulatory requirements in mind. Also the handling of (large) data sets and its validation is important.

In the afternoon an interactive workshop was held to discuss the present and future of R&D in drug development and how statistical departments and statisticians may evolve relative to skills sets, expertise, roles and responsibilities. Main items to develop or improve in terms of new and future activities is to take responsibility for evidence generation, be influential, but also be open to change. Operational feasibility (play with data attitude) is key to develop innovation and this should best occur in a collaborative, multi-disciplinary setting for cross-fertilization but still bring to the discussion the role of chance. On areas of influence and organization items to be developed or improved were to increase biostatistics activities

outside of traditional phase 2-3 studies, to increase statistical group capacity through training and make use of a more network-oriented organization to increase influence. Further areas like risk evaluation and probability of success were brought up as possibly helpful to increase influence.

The meeting was closed with suggestions for topics for the next meeting in 2017 as well as about its organization as the Chair, Stefan Driessen, has indicated to pass on the chair of organizing these successful series of Statistical Leaders Meetings to a successor.

All material from the EU Statistics Leaders Meetings are 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 2016 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 2016. Key highlights announced during the year included local association news and upcoming events. 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), Birgitte Biilmann Rønn (Treasurer), Egbert Biesheuvel (Scientific Affairs), Stefan Driessen (Statistical Leaders Meeting and SIGs), Chrissie Fletcher (Vice-President and Communications Officer), Christoph Gerlinger (Regulatory Affairs), and Julie Mellish (Executive Office).

Council Membership

In 2016, 10 countries national associations of pharmaceutical statisticians from 10 European countries were represented within EFSPI, totalising a combined membership of more than 2200 individuals.

Members of the EFPSI Council at the end of 2016 are listed in the Appendix.

Council Summary

Two Council meetings were held in 2016. 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 2016

Belgium
Emmanuel Quinnaux, IDDI
An Vandenbosch, Janssen

Denmark
Arne Haahr Andreasen, Andreasen Statistical Consulting
Birgitte Biilmann Rønn, Novo Nordisk

Finland
Sami Virtanen, Orion Pharma
Teppo Huttunen, 4Pharma

France
Emmanuel Pham, Ispen
Maylis Coste, Servier

Germany
Frank Langer, Lilly
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