EFSPI Statistical Leaders Meeting 26th May 2010

Discussion Notes

Executive Summary

The first EFSPI Statistical Leaders meeting that was held on the 26th May in Berlin. Representatives from all the European countries and major pharmaceutical companies were in attendance (full list of attendees attached). The purpose of the meeting was to develop a network of statistical leaders, shape and influence our professional environment and help to shape the strategy for EFSPI. In the first meeting, Professional development, assessment risk benefit assessment and health technology assessment (HTA) were discussed.

The Statistical leaders made a number of recommendations for initiatives and activities for the EFSPI Council to consider. These included: career development, skill development, organising meeting with other disciplines and fostering collaboration, linking IMI representatives and ensuring the wider statistics community are informed, forming special interest groups and developing resources for HTA. These recommendations will be discussed at the next EFSPI council meeting on 23rd June. Following the council meeting EFSPI will inform meeting attendees of proposed actions and will provide information for further communication.

Introduction

Nigel Howitt (EFSPI President) opened the meeting with an Introduction to EFSPI (slides below). He explained the objectives of EFSPI which are:

- To promote professional standards of statistics and the standing of the statistical profession in the pharmaceutical industry
- To offer a collective expert input on statistical matters to national and international authorities and organisations
- To exchange information on and harmonise attitudes to the practise of statistics in the European Pharma Industry and within member groups

The current 2010 goals include:

- Build a stronger European platform for statistical interaction
  - Statistical Leaders Meeting
  - European Conference of Pharmaceutical Statistics
- Use Statistical Leaders Meeting to develop our strategy for the future
- Deliver three quality European Statistical Meetings (Scientific Committee)
- Provide Cross-industry review of key regulatory documents (Regulatory Committee)
- Make more effective use of the EFSPI website

Lesley France introduced the purpose of the Statistical Leaders meeting which is to develop a forum for Statistical Leaders to:

- Network and share ideas
- Shape and influence our professional environment with respect to
  - Education & Continuing Professional Development
  - Methodology Development & Identification of Best Practice
  - Regulatory and Industry policies
  - Effective working with differing resourcing models
- Help to shape the strategy for EFSPI

And specifically in this meeting the objective was to

- To identify priorities for the strategic direction of EFSPI in
  - Professional Development for Statisticians
  - Evaluation of Risk Benefit
  - Health Technology Assessments.
- Identify experts who would like to be engaged in European initiatives

Statistical Leaders
EFSPI Presentation.p

<u>Professional Development for Statisticians</u>

Stephen Pyke introduced the topic of Professional development for statisticians assisted by Per Larsson as facilitator.

EFSPI HSM
Introducing Professio

There was a discussion regarding the obstacles which prevent statisticians being invited to undertake broad leadership roles, in some companies there is:

- A perception that broad / senior roles require medical qualifications.
- A culture that does not routinely encourage statisticians to take on broad leadership roles.

And/or

- Statisticians with strong leadership skills may lack visibility within organisations and with senior managers who are likely to appoint leaders.
- Reticence within statistical leadership, who do not want to lose the best statisticians from statistical roles.
- Statisticians themselves may be reluctant to take on wider leadership roles if this requires them to leave their area of expertise

To enable statisticians to operate effectively and be well positioned to fulfil wider leadership roles, it is recognised that it is important to develop, broad business awareness, drug development expertise, collaborative working skills to develop partnerships with other disciplines and a broad set of statistical skills. Quantitative thinkers, including statisticians, may be particularly well-suited to those leadership roles where dispassionate, rigorous, evidence-based judgement is needed. This also needs to be combined with a willingness to sometimes make judgements on the basis of incomplete evidence – in other words, to take calculated risks. There was some discussion about whether this was a typical characteristic of many statisticians.

It was agreed that acquiring the right skills is key to successful staff development. Development of leaders requires an appropriate focus from the start by providing work experiences and training (not focused on routine programming tasks) to ensure that they are developed/equipped to meet future challenges.

Company hiring strategy was also discussed. There was agreement that having a strong technical skill set was a necessary platform. However beyond that there was a shared concern that statisticians are perhaps too homogeneous as a group, with too few extroverted creative risk-taking types.

The following potential actions for EFSPI were discussed

- Identify training/best practice in developing broad drug development skills including:
  - Development of problem solving, communication and influence skills
  - Promotion of courses like the PSI Introduction to Industry Training (ITIT) course which provides broad development exposure in early career
  - Encourage member groups and companies to develop partnerships with local Universities to ensure students are equipped to meet Industry needs.
- Identify ways to enable the development of skills to support quantitative decision making, so that statisticians can support leaders in informed Decision Making.
- Take actions to support wide career paths for statisticians as drug developers by
  - Promoting career options and enabling the sharing of case studies for staff who have developed broad roles or who are influential in decision-making
  - Sharing existing and developing career paths material (possibly via the website, or else distributed to the membership). Suggestions include:

        - Producing a flow diagram/mind map to illustrate career options and paths
        - Development of suggested curriculum/ training track
- Identifying roles / business areas where Statistical skills can add the most value -- a top ten of opportunities where statistical contributions are most critical.
- Consider promoting professional accreditation of statisticians (as ASA, RSS are)
- Promote the role of statistics in drug development, demonstrating were statisticians are influential in their discipline. These promotion activities should go beyond late phase clinical trials (the classical role of pharma statistics) and into other areas across Research / Development / Commercialisation where statisticians are expected to play a more prominent role in future (e.g., HTA, portfolio management, quality assurance, in- /out-licensing).
- EFSPI should consider option for organising meetings with other disciplines e.g. Physicians, HEOR
- EFSPI should consider how it embraces a community of statisticians and statistical skills beyond clinical trials.

The priority areas identified for EFSPI from this discussion were

- Take action to support wide career paths drug developers by
    - Promoting career options and enabling the sharing of case studies for staff who have developed broad roles or who are influential in decision making
    - Sharing existing and developing career paths material either by the website or distributed to the membership. Suggestions include:
        - Producing a flow diagram/mind map to illustrate career options and paths
        - Development of suggested curriculum/ training track
- EFSPI should consider option for organising meetings with other disciplines e.g. Physicians, HEOR

If EFSPI council are in agreement it is proposed that the statistical leaders would share:

- At least one case study of a member of staff's career path by end July.
- Information on career paths

So that EFSPI to produce a career map for statisticians which illustrates potential career paths.

Assessment of Risk Benefit

Juergen Kuebler introduced the topic of Assessment of risk benefit assisted by Thorkild Nielsen as facilitator.

EFSPI HSM - Introducing Benefit-R

There was discussion regarding the Innovative Medicines Initiative (IMI) – Protect which is addressing risk benefit. This is at the beginning of a 5 year pieces of work to improve the methods and approach to risk benefit. There are a large number of groups engaged with this initiative and there is a network of experts working within the project. It would be useful to the wider industry to have greater visibility of the individuals engaged in this work and awareness of the activities and plans. It would also be valuable to develop a forum for the quantitative sciences engaged in the IMI initiative.

Action: All share names of people involved in IMI

There are many different perspectives on the assessment of risk benefit including: Patient, Payer, Regulator, Physicians. It is unlikely that one solution will meet all the needs so analysis methods and integration of information will be required to be flexible.

An EFSPI action could take in this area is to link company IMI statistics representatives to provide information on the IMI activities to the wider community (IMI | The Innovative Medicines Initiative(www.imi-europe.org)).

Risk benefit is an area where statistical profession has an opportunity to lead change. EFSPI could form a special interest group comprising the IMI PROTECT representatives and other interested individuals.

If EFSPI is going to form special interest groups they need to develop a framework for these groups and provide a way for member groups to initiate this type of activity.

US PhRMA (www.PhRMA.org) formed the BRAT group and produced a publication on risk benefit. It is proposed that EFSPI form an interested group to develop a European publication on the current state of the art.

Throughout the meeting there was discussion on increasing the links between EFPIA and EPSPI. EFPIA is engaged in this IMI initiative and to be effective it will be important for EFSPI to collaborate with EFPIA. EFSPI should investigate if EFPIA has set up a risk benefit group. Now that there is an EMA statistic working group EFSPI should investigate if EFSPI could be the link to the EMA working group under the EFPIA banner.

There was considerable discussion about the disparity between efficacy and safety analysis and the reasons for lack of more through safety analyses were discussed. Suggestions for potential reasons for lack of safety evaluation included, lack of familiarity with techniques and lack of awareness of the

broad business requirements. It was pointed out that it is our obligation to do more for safety and the REMS requirements is an outcome of the insufficient activity in this area.

The industry statisticians need to increase their skills to undertake this type of work and those of the project statisticians to understand the changing environment. EFPSI could assist this by:

> Provide training for project statisticians on: epidemiology methods, understanding the physicians approach to safety evaluation (e.g related variables) so that they are able to identify the important questions, predictive safety methods, use of graphical review tools, working in and influencing multi-disciplinary teams.
>
> Providing tools for managers to enable them to provide the key messages within their business on risk management e.g. Interrogation of cumulative safety data to improve quantify risk better

There was a discussion concerning how best to organise risk benefit support within companies. Two main options were discussed, as a specialist group or as part of the ongoing job of project statisticians. There was general consensus on the need to have experts as consultants to enable re-skilling and driving the development of methodology. It was recognised that there is a need to have safety and efficacy aligned; different companies achieve this with different operational models.

The use of internal and external experts can help improve the assessment of risk benefit. Questions were raised as to whether statisticians routinely accessed appropriate internal and external expertise. Increased alignment of quantitative skills with greater collaboration has been seen to be beneficial. Activities to increase this type of collaboration can aid the provision of information to better inform decision making.

Discussion with the regulatory and payer environment is changing the emphasis from efficacy evaluation to effectiveness. Evaluation of effectiveness makes use greater use of observational data. Effect sizes may be smaller in observational data because the environment is not as controlled. As a profession we should maintain awareness of comparative effectiveness research.

The paper Relative efficacy of drugs: an emerging issue between regulatory agencies and third party payers. Nature Hans George Eichler et al. was circulated (attached below)

Eichler et al Nature Review 2010 Relative

The priority areas identified for EFSPI from this discussion were

- Link company IMI statistics representatives to provide information on the IMI activities to the wider statistics community
- Undertaking activities to lead change in the Risk benefit area. In particular EFSPI could form a special interest group comprising the IMI PROTECT representatives and other interested individuals.

- Formation of an interested group to develop a European publication on the current state of the art of Risk Benefit.
- The industry statisticians need to increase their skills to undertake this type of work and those of the project statisticians to understand the changing environment. EFPSI could assist this by:
  - Provide training for project statisticians on: epidemiology methods, understanding the physicians approach to safety evaluation (e.g related variables) so that they are able to identify the important questions, predictive safety methods, use of graphical review tools, working in and influencing multi-disciplinary teams.
  - Providing tools for managers to enable them to provide the key messages within their business on risk management e.g. Interrogation of cumulative safety data to improve quantify risk better

Health Technology Assessment (HTA)

Chrissie Fletcher introduced the topic of Health Technology Assessment assisted by Christoph Gerlinger as facilitator.

EFSPI HSM
Introducting HTA fina

There was a discussion about how early statistician should engage in HTA. Early engagement is important to allow development of PROs required for later phase work and to ensure phase III designs appropriately address HTA issues and data. Early discussion with payers helps to identify key design features (e.g. comparators, outcome measures) to be built into the program design.

There seems to be two models for HTA delivery one involving different HTA specialists and the other with a more broad role approach. If there are separate statistics groups, it will be important to work together collaboratively. Where there are different groups, formation of communities of interest has proved valuable e.g. (PRO interest community, Epidemiology interest community).

The question was raised as to whether our existing statisticians are sufficiently skilled? There are many local HTA local policies but no global guidelines. As with risk-benefit engagement with different skills groups and working collaboratively are important for success. HTA activities use a different language and investment of time in understanding the language is essential. Need to engage with others

Good sources of information for HTA are the guidance documents – Canada UK Australia, Germany. NICE have open meetings and people can go and observe the proceedings.

Also PSI created a HTA handbook which provides links to these documents and additional information on HTA (including information on training courses).

Link to HTA Handbook

EMA and EUnetHTA are working together on relative effectiveness to improve the EPAR (started in Feb)

The PSI have a Special interest group on HTA, it is proposed to broaden this to an EFSPI Special interest Group.

Action: Identify people who would like to engage in the HTA sig

As this is a developing area, it would be useful if EFSPI would develop resources on HTA

As with risk benefit in order to support HTA it is important to have collaboration across the disciplines. Particular areas for the application of statistical expertise are: Network Meta Analyses (including indirect and/or mixed treatment comparisons), understanding of the HTA modelling approaches, PRO validation, extrapolation of effects, evaluation of the level of uncertainty and sensitivity analysis, use of Bayesian approaches and probabilistic analyses.

Is it reasonable for one statistician to do all? How can the statisticians take this on? It is recognised that they need to effectively access experts skills and know where and how to connect these experts. Communicate and collaborate skills are key. Strategic statisticians should be a facilitator for the internal and external experts

NICE are funding research on combining clinical trials and database/epidemiological data

EFPSI look into who we could best collaborate with other skills professional bodies.

There are huge opportunities to influence the methods development. The IPSOR task force last year did not engage statisticians from EFPSI on their Indirect Comparison Good Practice taskforce, this was a missed opportunity. Other areas for improvement are the use of incremental cost effectiveness ratios which have inherent statistical issues due to being a ratio as opposed to use of other parameters with better statistical properties.

The priority areas identified for EFSPI from this discussion were

- Broaden the PSI Special interest group to an EFSPI Special interest Group.

Action: Identify people who would like to engage in the HTA sig

- Develop resources for HTA and make available to member groups
- EFPSI look into who we could best collaborate with other skills professional bodies.

Summary of meeting

Actions:

1. Send out slides and paper by the end of the week – Thorklid **done**

2. Draft notes of meeting circulate to presenters and facilitators by end of week. – Lesley **done**
3. Presenters and facilitators review by end of next week **done**
4. Send revised notes with an executive summary out to all participants by mid June
5. Send out survey to participants on the meeting content and conduct by mid June.
6. Create a communication slide set for the leaders to use
7. Discuss with EFSPI council on 23rd June
8. Feedback to this meeting after the EFSPI council meeting

There was consensus that the meeting was useful and participants would like to see this as an annual event. Suggested topics for future meetings are:

- Continue discussion on professional development
    - How we can develop the stat leader of the future
    - Where will talent pool (new stat) come from in the future
    - Take broader role of "statistics" and not "statisticians"
- Modelling and simulation
- Epidemiological/observational research
- Translational sciences
- Identify any areas where we need to engage statistics more
- Engagement with KOLs, being an expert and bringing in expertise and understanding both are important
- Out-reach to other organisations, e.g. IMI, EFPIA, others?
- Emerging regulatory/payer guidance
- Linking this forum with US and other Global Heads of Statistics Departments

Meeting Attendees

Name	Company	Country
Egbert Biesheuvel	SPCORP	Netherlands
Frank Bretz	Novartis	Switzerland
Hans Ulrich Burger	Roche	Switzerland
Florence Casset-Semanaz	Merck Serono	France
Maylis Coste	Servier	France
Stefan Driessen	Solvay	Netherlands
Christine Fletcher	Amgen	UK
Lesley France	AZ	UK
Christoph Gerling	Bayer Schering Pharma AG	Germany
Kerry Gordon	Quintiles	UK
Nigel Howitt	PRA Int.	UK
Sara Hughes	VIIV	UK
Niels Michael Kamp	Novo Nordisk	Denmark
Oliver Keene	GSK	UK
Olavi Kilkku	Orion Pharma	Finland
Juergen Kuebler	Novartis	Switzerland
Per Larsson	Novo Nordisk	Denmark
William Malbecq	Merck Sharp & Dohme Europe	Belgium
Paolo Morelli	CROS NT	Italy
Thorkild Nielsen	Bayer Schering Pharma AG	Germany
Stephen Pyke	Pfizer	UK
Jamie Robinson	Roche	Switzerland
Martin Struijs	Genzyme	Netherlands
Stig Johan Wiklund	AZ	Sweden
Josephine Wolfram	Astellas	Netherlands