IABS – Contribution to Success Stories

For more than 60 years, IABS (International Alliance for Biological Standardization) has had a major impact on scientific and regulatory processes worldwide. These contributions have occurred primarily through collaborative scientific meetings and publications in the journal *Biologicals.* IABS' unique role and strength reside in its ability to bring together interested parties for scientific discussions of important unresolved or emerging issues, to assist in developing a consensus and an action plan to achieve regulatory progress. This strategy has led to significant gains in both the human and veterinary fields, and it differentiates IABS conferences from most scientific meetings that focus simply on the exchange of information. IABS is unique as a nonprofit neutral organization dedicated solely to addressing key issues in regulatory science that underpin approvals for vaccines and biopharmaceuticals worldwide. Together, with our conference partners and collaborators (private industry, academia, regulatory officials) we have held a variety of conferences on a broad spectrum of topics concerning the biological and biopharmaceutical arena, as well as the veterinary and human health fields. Another unique aspect of IABS conference is the final session which is dedicated to drafting consensus meeting summaries, conclusions & recommendations which are subsequently made available interested parties such as regulatory agencies and the biological and biopharmaceutical industries. These recommendations have had a positive impact on the regulatory process in many cases. Significant achievements and the positive impact that these recommendations have had on regulatory processes are outlined in each of four scientific areas are outlined below.

Examples of Contributions to Scientific and Regulatory Progress through IABS Scientific Conferences, Workshops and Symposia:

<u>Biotherapeutics</u>:

Starting in 2014, the IABS Biotherapeutics Committee has built the joint FDA/IABS *Stats & Data Management Approaches for Biotechnology Drug Development* workshop into an annual event which has become the reference among meetings of its type. At its outset, the Stats & Data meeting's main target was statisticians supporting CMC applications in biotechnology development. Word spread of the value of the meeting so that today, participants include well-recognized industry and regulatory statisticians *and* those who are seeking guidance on how to use statistics for the work they conduct during biotechnology and vaccines product development. This has likewise extended to statistical and data management opportunities in commercial manufacture and quality control and the evolving arena of biosimilars. The well-designed agenda offers the expert guest speakers an opportunity to share their knowledge and experience regarding the use and management of statistics and, through exchange and discussions with the participants, to gain new knowledge and perspectives which will then serve to inform the guidelines they draft for the use of statistics in drug development.

Recent Biotherapeutics Committee Meetings:

a. **2013** - Setting Specifications for Biotechnology Products: Facing Evolving Challenges Chair: Tony Mire-Sluis. Co-organizers: IABS / Food and Drug Administration

b. **2014** - Statistical and Data Management Approaches for Biotechnology Drug Development. Chair: Tony Mire-Sluis. Co-organizers: IABS / Food and Drug Administration

c. **2015** –

   i. 2nd Statistical and Data Management Approaches for Biotechnology Drug Development. Chair: Tony Mire-Sluis. Co-organizers: IABS / Food and Drug Administration

   ii. 2nd Progress and Challenges in Protein Particles and Immunogenicity of Biotherapeutics 2015: Filling in the Gaps in Risk Evaluation and Mitigation. Chair: Tony Lubiniecki. Co-organizers: IABS / Health Canada

d. **2016** - 3rd Statistical and Data Management Approaches for Biotechnology Drug Development. Chair: Tony Mire-Sluis. Co-organizers: IABS / Food and Drug Administration

e. **2017** – 4th Statistical and Data Management Approaches for Biotechnology Drug Development. Chair: Tony Mire-Sluis. Co-organizers: IABS / Food and Drug Administration

The Biotherapeutics Committee has also organized in the past years two conferences on Protein Particles and Immunogenicity of Biotherapeutics. One key outcome of the first meeting was the consensus that standardization of quantitation technology was needed as there were clear gaps in understanding how some types of particles might relate to immunogenicity and whether this applied to all types of protein particles in all biotherapeutics. A second meeting was therefore organized to further the discussion with the goal to assess the progress of the past half-decade, and its implications for risk management during biotherapeutic product development. The meeting generated considerable interest and for the first time, poster presentations and tabletop displays were organized during the breaks. The success of the meeting was such that there was general request for a follow-up meeting within the next 2 to 3 years.

Cell Therapy:

Cell therapy is an emerging therapeutic area where research and development, including clinical studies, have been ongoing in both developed and developing countries. A variety of regulations and guidelines have been published or are in development by governmental organizations in different regions of the world. In addition, professional organizations have provided guidance for professionals working in the field. Although there are common elements in the various guidance documents, there are also differences among them which have led to significant regulatory challenges and uncertainty. As a result, there is a clear need for a global effort to develop a set of common principles that may serve to facilitate a convergence of regulatory approaches to ensure the smooth and efficient evaluation and regulation/surveillance of products and production facilities based on sound scientific principles.

Identifying a core set of principles would be useful in the initial drafting of a WHO guidance document, and WHO has encouraged IABS to provide opportunities to explore issues in cell therapy, and to publish meeting reports and recommendations for consideration at the point when a WHO guidance document will be developed.

To initiate the process of developing a global document on this subject, a workshop jointly sponsored by IABS and the Japan Science & Technology Agency (JST) was held in Kyoto, Japan on 7-8 March 2014 to discuss challenges toward the sound scientific regulation of cell therapies.

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A follow-up conference jointly sponsored by the WHO, IABS, Pharmaceuticals and Medical Devices Agency of Japan (PMDA) and JST was held in Tokyo, Japan on 18-19 February 2015, and was attended by experts from academia, regulatory and control authorities, and industry involved in the research, manufacture, and approval of cell therapies from countries around the world. The purpose of the meeting was to review the available scientific information and data, and to identify and discuss the most significant current regulatory issues in the field of cell therapy.

Problem areas that were identified include: a) potency tests which have functional readouts and are not dependent on surrogate markers; b) tumorigenicity tests and the need for international standards for control cells; c) the point at which, and extent to which, GMPs should apply. The conference also concluded that WHO is the preferred international organization to take the lead in developing international guidance, and that work should be initiated on the development of a rational regulatory framework for cell therapies that could be used as a starting point for WHO to develop an international guidance document.

A subsequent, independent (non-IABS) international regulatory forum on human cell therapy continued discussions on the challenges raised at the IABS 2015 conference. The forum was held in Osaka, Japan, on March 16, 2016. Over 300 participants from regulatory agencies, non-governmental organizations, academia, and industry in North America, Europe and Asia attended the forum. At this conference, it was suggested that a useful approach to the scientific evaluation of cell therapy products (CTPs) would be the development of a minimum consensus package (MCP) as the cornerstone for a global guidance document. An MCP would encompass scientific principles/concepts, general considerations, and common core technical requirements generally applicable to most CTPs, and it could serve as a common platform for interested parties. It was emphasized again that there is a need for a global best practices document regarding the evaluation of quality, efficacy, and safety of the CTPs to minimize inconsistency in regulatory approaches among interested parties and to promote international regulatory convergence through an international organization such as WHO.

The most recent IABS conference on cell therapy was held in London on 2-3 November 2016. The conference focused on key issues for the manufacture of cell therapies and provided scientific consensus on selected aspects to inform the drafting of future guidance. As with previous IABS meetings, this one aimed to bring together representatives from industry, academia, health services and regulatory bodies. The program covered recent developments in regulation, registries and banking of stem cell lines, requirements for raw materials, manufacturing, standardization, characterization and preservation.

Relevant reports of IABS Cell Therapy meetings were and will be published in 'Biologicals'. IABS will continue to work towards the development of core regulatory elements that could lay the foundation for a WHO guidance document for cell therapy.

Human Vaccines:

Update Pending

Veterinary Biologicals:

For quite some time, vaccines for minor species and/or minor indications (MUMS – also termed minor market products) were neglected in Europe. In 2003, an IABS meeting (Langen, Germany)

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drew attention to this issue. The discussions and conclusions influenced not only guidelines drafted by the European Medicines Agency, but also the legislation in Europe.

In 2007, a meeting in Paris co-sponsored with OIE and other organizations drew attention to the role genomics can play for animal health. Major topics were: quantitative population studies to identify markers of health traits, functional genomics of host-pathogen interactions and translating genomic information to tools for controlling diseases. The proceedings published in the IABS series *"Developments in Biologicals"* include key recommendations for moving forward and serve as a roadmap for future research initiatives.

The IABS meeting that was held in Annecy (2010) on "**Viral Safety and Extraneous Agents Testing for Veterinary Vaccines**" has now started to influence the legislation. In February of 2013, revision of extraneous agents testing was started at the European Pharmacopoeia. This Discussion is expected to take time, but is has started. The starting point of these revisions were the discussions at this workshop in Annecy. With regard to EMA, the extraneous agents testing is under discussion as well in cooperation with the International Federation of Animal Health (IFAH). The discussions in Annecy also have had an impact within EMA and Ph.Eur.

The Meeting: "**Potency Testing of Veterinary Vaccines: The Way from *in vivo* to *in vitro*"** was held at the Paul-Ehrlich-Institut (PEI) in Langen. It was co-sponsored by PEI and the European Directorate of the Quality of Medicines (EDQM). The meeting contributed significantly to the efforts to replace *in vivo* testing of vaccine batches by in vitro methods. Two positive effect should be mentioned: USDA first time accepted and *in vitro* test for antigen quantification as in process tests for rabies vaccines. In addition, a company offered to share its data with other laboratories, working on the replacement of *in vivo* tests. The meeting report was issued in Biologicals Vol 40, 1, 100-106, 2012: J. Romberg, S. Lang, E. Balks, E. Kamphuis, K. Duchow, D. Loos, H. Rau, A. Motitschke, C. Jungbäck: Potency Testing of Veterinary Vaccines: The Way from *in vivo* to *in vitro*.

In 2016, a meeting on *Emerging Infectious Diseases of Animals: Strategies in Surveillance, Control and Eradication* was held in Budapest, Hungary. IABS along with the Hungarian *National Food Chain Safety Office Directorate of Veterinary Medicinal Products* collaborated to bring together international participants to discuss how emerging infectious diseases challenge the health of domestic and wild animals and humans irrespective of political and geographic borders. In addition to presentations on licensing procedures for novel vaccines for emergency use, novel surveillance, diagnostic and control strategies, lectures also addressed environmental factors affecting disease outbreak and spread, impacts of disease on national economies and the global safety and security of food products. The recommendations and conclusions of the meeting led to a proposal on update of the EU-legislation to allow quicker licensing for vaccines in the context of outbreaks of emerging newly occurring diseases.

Note: If you are interested in a comprehensive list of IABS-sponsored Conferences, see separate addendum listing IABS Conferences, Workshops, and Symposia.

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