

# ESTP Newsletter 2014 (3)



*Editor Zuhai Dincer (zuhai.dincer@novartis.com)*

## President's column



Dear ESTP members,

It is with great pleasure that I write my first President's column for the ESTP. The annual meeting in Berlin held between the 27<sup>th</sup> and 30<sup>th</sup> August, in conjunction with the ECVF and ESVP was an enjoyable and stimulating meeting. Comments expressed to me during the meeting and since then, have conveyed a feeling of high scientific quality and excellent organisation. We appreciate all feedback and look forward to reviewing all your feedback comments at a future Executive Committee (EC) teleconference. We strive to take on board comments from the membership in order to ensure we can maintain the success of our annual meetings. The extra dimension this year of having our veterinary diagnostic contemporaries in attendance enabled those working on both sides of the fence to benefit from the talks and experiences of other colleagues. The poster sessions, as well, revealed to me that a number of academic research projects in veterinary pathology continue to be highly applicable to the toxicologic pathology field. I hope you all came away with greater

understanding, new friends and colleagues to collaborate with, and felt invigorated to face the challenges ahead in our profession. For that, we have to extend our thanks to the Scientific Organising Committee and Local Organising Committee led by Anna-Lena Frisk and Achim Gruber. A special thanks must also go to our former chairman Frédéric Schorsch who provided leadership and guidance throughout his chairmanship, and, of course, will continue to be actively involved in the Executive Committee. My thanks to Frederic for providing a steady ship for me to steer! We also welcomed a number of new members to the Executive Committee including Gabriele Pohlmeier-Esch as the Secretary, Lars Mecklenburg as our Vice Chairman, Annabelle Heier as the Councilor for the Younger generation and Hans Harleman as the IFSTP representative. We are also fortunate in having two roles which indicate the increasing importance of technology in our communications and daily work. These are Thierry Flandre as Councilor of Telepathology and Rupert Kellner as Councilor for Electronic Communication. An additional thanks must go to our long-serving secretary Francesco Marchesi who provided diligent and careful service during his years as Secretary. Francesco, we wish you well in your new endeavours! If you were not in Berlin, the member section of our website informs you about the presentations and our discussions. The minutes of our Annual General Assembly are also available. Thanks to Rupert! We already look forward to next year's conference held together with the BSTP in Surrey and ably being co-ordinated under the direction of Aude Roulois on behalf of the ESTP and Franck Chanut on behalf of the BSTP.

### **1. Greater involvement in European and international initiatives**

It is just over one year ago that Food and Chemical Toxicology published an article by Seralini *et al.* The article reported erroneous interpretations of a 2-year feeding study in rats investigating the health effects of genetically modified maize. In response to this, a letter

was sent to the editor of Food and Chemical Toxicology summarizing comments from the ESTP EC to highlight the major toxicological pathology shortcomings of the article. This was a key example where the ESTP can take an active role in educating and correcting erroneous data presented on the broader European stage. Our rapid and strong reaction emphasizing the need for best practice in toxicologic pathology was recognized by the European Regulatory Authorities. As a consequence, ESTP is today considered as a stakeholder in the discussions on the long term toxicity studies for health risk assessments of GM food initiated by the European Commission and national authorities. Two members of the EC, myself and Wolfgang Baumgartner, sit on the current advisory panel and it is a tribute to the work of the ESTP that we are recognized as key contributors in such initiatives.

The ESTP also has three core international initiatives which include our collaborations within the INHAND, SEND and RITA initiatives; all are seen as very important contributions our society can make to our discipline, and increase our profile. The Classic Examples in Toxicologic Pathology also remains popular and particular thanks goes to Thomas Nolte.

This year also saw the society working with new initiatives including the “scientific and medical writing” initiative driven by Lars Mecklenburg, who organized a highly interesting satellite workshop during this conference. Concerning the future vision of our profession, the new committee “Pathology 2.0”, led by Franck Chanut, has many new ideas on how to improve the role of toxicologic pathology in drug discovery and development, by using new technology and techniques of risk assessment. A second new committee, “Clinical Pathology and Biomarkers”, led by Aida Diaz-Bayon, seeks to improve links with the Clinical Pathology community. There is also a very recent initiative to work on the definition of adverse effects, by Gabriele Pohlmeier-Esch and Wolfgang Kaufmann (please see their article in this newsletter).

## **2. Greater involvement of younger pathologists in the ESTP**

As I walked around the conference feeling like a rather sprightly 40+ year old person, it suddenly dawned on me that I was now in the middle age! The days of sitting as a student/trainee/new kid on the block were long gone and there was a new generation out there who would look up to old folks like myself for guidance. It is important that the new pathologists and those in training learn more about the toxicological pathology industry. The dual conference with our veterinary pathologists no doubt opened the eyes of some of those involved in veterinary pathology to toxicologic pathology. However, it is a sad fact that sometimes we do not promote our own profession to those upcoming vets in training. This was one of the points of discussion at the Presidents Luncheon Meeting in Berlin and there are certainly new

initiatives and ideas being discussed within the STP for webinar training, sharing of such training initiatives between the different societies and even outreach to veterinary undergraduates, not only those already in postgraduate pathology training. The ESTP EC is working together with other societies on these initiatives. It was a pleasure to recognise the work of new colleagues at our Congress in the Thesis awards distributed to 1st: Alexandru-Flaviu Tabaran, “The Biodistribution, Toxicity and application of carbon nanotubes in cancer therapy, 2nd: Lieve Vangeel, “Bovine Sarcocystis species and their role in Bovine Eosinophilic Myositis and 3rd: Yanyong Sun, “Role of JAK-STAT signaling in the pathogenesis of astrogliosis in chronic demyelinating Theiler's murine encephalomyelitis”.

## **3. Who is the new President?**

I would like to thank you again for your trust in me in the President's role for the next two years. Someone asked me at the conference, so what can you bring to the President's role? No one person can know everything, but the professional experience that I bring to my role are an initial background of eight years in diagnostic veterinary pathology, followed by 12 years in the pharmaceutical industry, and a return now to management within an organisation working primarily, though not exclusively, in diagnostic pathology. I became the first UK person to pass the ECVP Board examination in 2000, and then spent 7 years on the ECVP Exam Committee working with wonderful colleagues and seeing that organization and the establishment of its exam taking off, with recognition of equivalent status to the ACVP exam. Moving in parallel with that, was the establishment of the ESTP and the growth of its membership, currently at 306. I feel privileged to have seen both organizations created, established and grow to international recognition. These were indeed exciting times in European pathology. Additionally, through work between our society, JSTP, IFSTP and others, during my membership of the STP Scientific Regulatory and Policy Committee (and now with Annette Romeike as our European representative), I grew a large network of colleagues and friends across the continents and disciplines, and I look forward to working with them again in my President's role. Above all, I will bring commitment, dedication and of course, a strong sense of humour! I am fortunate to be working with a strong team of people bringing diverse talents to the ESTP and together, that team, looks forward to the many opportunities ahead where we can influence and work with others to promote and enhance the science of toxicological pathology. Thank you to all of them for the giving of their “spare” time and many hours of work to the organization.

Finally, we can only be as active as the sum of all our members, and I would encourage you all to participate in the society's initiatives such as “Guess What” run by Susanne Rittinghausen on our website, also contact the

EC with any ideas you may have on how we can support your needs, and also think of ways the ESTP and its conference can be made more widely known through work with related societies such as EUROTOX and our exhibition sponsors.

Thank you for your membership and support.

**Jenny McKay**  
**Your Chairman**  
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## **Joint Meeting of the European Society of Toxicologic Pathology (ESTP), European Society of Veterinary Pathologists (ESVP) and European College of Veterinary Pathologists (ECVP) in Berlin, Germany**



From August 27<sup>th</sup> to 30<sup>th</sup>, 2014, the “Cutting Edge Pathology” Congress took place for the second time as a joint meeting of ESTP, ESVP and ECVP at the Estrel’s hotel in Berlin, the biggest hotel in Germany. More than 400 participants from all continents attended the exciting conference program, which comprised interesting talks about toxicologic, diagnostic and experimental pathology. Key topics from the ESTP were the toxicopathology of the endocrine organs with special emphasis on endocrine disruptors of the reproductive system, as well as a session on nanopathology. Highlights from the ESVP/ECVP were the Key Note Lectures on the European Pathosurveillance Network and animal disease control and on predictive tools in animal cancer, pathogenesis of spinal cord injury and development of cell-based therapies. A “Mystery Slide Session” of skin pathology cases was arranged by the International Society of Veterinary Dermatopathology (ISVD).

On the first conference day, the ESTP introduced a novelty with a well-received workshop, organized by Lars Mecklenburg. This pre-meeting session, presented

by Karin Jochims and Barry Drees, aimed to give tips for scientific writing for toxicopathologists, for regulatory dossiers and for communicating large data sets. Wednesday afternoon was filled with interactive sessions about the most recent INHAND publications, on the reproductive and endocrine systems. This half-day might even need an extension of its time slot as passionate discussions about nomenclature happened, especially on hypertrophy versus hyperplasia of the adrenal cortex.



The welcome reception on Wednesday evening in the foyer of Estrel’s hotel was the official opening of the “Cutting Edge Pathology” with speeches of each Society’s president (Frédéric Schorsch for the ESTP, Carl Hård af Segerstad for the ESVP and Sean Callanan for the ECVP).



Thursday started off with the Key Note Lecture by Tom Rosol with exciting examples of endocrine pathology from history, art, and the microscope. This ranged from the most recently discovered hormones FGF23 and betatrophin up to examples of historical paintings depicting people apparently suffering from endocrine pathologic conditions. Duncan Ferguson gave an overview of thyroid pathology in the different lab animal species and illustrated the relevance of thyroid disruption in animal models. Sybille Gröters presented large datasets from rodent studies, aiming to elucidate the endocrine disrupting effect of anti-androgenic chemicals occurring in the environment. The BSTP-sponsored

Chirukandath Gopinath lecture was given by Dianne Creasy, with an outstanding overview of the male reproductive system, for which she received the award from Dr. Gopinath himself. Niels Skakkebaek presented his clinical research about male infertility and the possible effect of endocrine disruptors on low fertility rates and thus its effect on demographics. Next talks by Karen Mandrup about her work on endocrine disruptors in the rat and by Hans Harleman on evaluation of the mammary gland in safety studies.

Friday morning covered the pituitary and adrenal gland by Tom Rosol and the female reproductive system by Justin Vidal. Both presenters greatly combined embryology, histology, physiology and pathology. The remaining time was dedicated to the placenta with Maria Cecilia Rey Moreno and Eberhard Buse sharing her experience in rat placenta pathology and Eberhard Buse his expertise on the non-human primate placenta. Ann Hubbs gave a comprehensive Key note Lecture on the challenges of nanotechnology for the toxicologic pathologist.



On Friday evening, the congress dinner took place in a German brewery-style restaurant in the centre of Berlin where decent beers were served around the dinner. Afterwards the sweeping sounds of a fantastic band were inviting to the dance floor until late after midnight.

The Berlin conference ended Saturday morning with toxicologic and diagnostic pathology case presentations, during which the audience was asked to diagnose interesting and rare pathology cases using an electronic voting system. The following work received special recognition:

Two poster prizes were awarded by the French Society of Toxicologic Pathology (SFPT), of 1000 Euro each. The prize for the best poster was given to the poster presented by Grégory Hamm et al. for “Assessment of drug toxicity in small histological structure of the eye: application of mass spectrometry imaging in ophthalmic context” and the poster prize young scientist went to Tânia Carvalho for her work “Metabolic shift in cancer cells: insights from an acute leukemia xenotransplantation model”. The ESTP thesis awards went to: 1<sup>st</sup> prize to Alexandru-

Flaviu Tabaran “The biodistribution, toxicity and application of carbon nanotubes in cancer therapy”, 2<sup>nd</sup> prize to Lieve Vangeel “Bovine Sarcocystis species and their role in Bovine Eosinophilic Myositis” and 3<sup>rd</sup> prize to Yanyong Sun “Role of JAK-STAT signaling in the pathogenesis of astrogliosis in chronic demyelinating Theiler's murine encephalomyelitis”. Recipients of the Trainee Awards, offered by the International Federation of Societies of Toxicologic Pathologists (IFSTP), were Jana Keller “Comparison of pulmonary inflammation after short-term (5 days and 4 weeks) inhalation exposure to CeO<sub>2</sub> nanoparticles based on analysis of bronchoalveolar lavage fluid and histopathology “and Laëtitia Dorso “CD105 expression and usefulness of its targeting for antivascular alpha immunotherapy in a mouse model of breast cancer”.

Also part of the congress social events allowed us to deepen relationships with colleagues, friends and speakers. All along the congress, the local organizers did offer sightseeing tours of the historic city of Berlin, such as a tour of Berlin underworld, the museum of medical history, a boat tour and a guided tour of the vet school. The local organizers Anna-Lena Frisk from Bayer Pharma AG, Berlin, and Achim Gruber, from the veterinary pathology department at the Free University Berlin, together with a large team of helpers, did a tremendous job organizing this successful congress.

Next year, the congress (September 22-25<sup>th</sup>, 2015) will take place in collaboration with the British Society of Toxicological Pathology (BSTP) in Surrey, UK, entitled “From genes to drugs: an insider's view on cell pathology”. We hope to see many of you again.

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### **Impressions on Scientific Writing Workshop for Toxicopathologists at the Joint Meeting of ESTP, ESVP and ECVF in Berlin, Germany**

On the last ESTP congress in Berlin there was a 4-hour workshop on “Scientific writing for toxicopathologists” in the morning before the regular congress started. This workshop was kindly organized by Lars Mecklenburg. Two excellent speakers were invited: Dr. Barry Drees from Trilogy Writing & Consulting based in Frankfurt/Main, Germany, and Dr. Karin Joachims from IASON consulting based in Niederzier, Germany.

In the first two hours, Barry -in a stimulatory and vivid presentation style- strengthened to determine the message and the audience before writing the documents. He said No one will read scientific documents in a

comfortable chair on a cold winter's night but rather go directly in certain parts of the document to look for special information. He recommended the deductive or in his words" Columbo" writing style with the message up front and then taking the reader through the logic of why the data were interpreted to produce that message. For this reason, such as lists, flow charts, tables and figures might be more helpful for the reader to understand the data and interpretation than written text.

In the second two hours, Karin gave her presentation alternating with short practical exercises to be discussed in groups. She pointed out that there is no commonly agreed definition of the NOAEL across different guidelines and papers. In the following examples this was also a point of controversy and suggested as another topic for an upcoming workshop (please see below article by Gabriele Pohlmeier-Esch & Wolfgang Kaufmann in this newsletter). By dealing with large pathology data sets, she strengthened the importance of having extra information beside the pathology data if possible to make a thorough evaluation and concise interpretation at the end. The pathology data itself should be discussed in an integrative way with data from clinical pathology, gross pathology and organ weights in context with histopathology. Since for most regulatory documents the readers will not be pathologists, the terminology and interpretation should be clear and without uncertain terms.

Overall, this was an interesting workshop in a good atmosphere with a lively and valuable discussion with the lead of two excellent speakers and great participation of audience. It would be very much appreciated if such a workshop could be organized for the upcoming congresses again.

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### **Proposal for the new series of ESTP International Expert Workshops to differentiate adverse from non-adverse organ effects**

Dear ESTP members,

During the Annual General Assembly 2014 in Berlin we presented our idea to launch a new series of ESTP International Expert Workshops, in order to differentiate adverse from non-adverse organ effects in toxicity studies by organ system and species. Endorsed by the Executive Committee this project was very welcomed by the membership.

As we all know, study pathologists are increasingly challenged to define a «No-Observed-Adverse-Effect-

Level» in toxicity studies, based on results in pathology. The need for clear criteria and for a clear communication of these effects has been recognized internationally.

Recently, a working group of the STP Scientific and Regulatory Policy Committee has elaborated a general recommendation of practices for defining and communicating adversity for nonclinical study data, however, the term "adverse" has still not been concurrently defined.

Our society already has experience in the organization of International Expert Workshops, the latest one defining adversity or non-adversity of hepatocellular hypertrophy. With the aim to set standards for the argumentation within pathology reports and with regulatory authorities, these workshops were made up of international experts in the field, from Europe, the United States and Asia, and led to publications in internationally recognized peer reviewed papers.

Following these examples, the future series of «International ESTP Expert Workshops» should be organ-specific and deal with lesions frequently encountered in routine toxicity studies. For each of these lesions, clear criteria for the differentiation of adversity from non-adversity should be worked out. It was pointed out during the AGA that the clear definition of the term "adverse" should be one of the first steps in this series.

To add an important educational aspect, the workshop discussions could (partially) be opened to interested society members, possibly via webinar technology. We will also look into the possibility to share scanned slides. We are currently collecting topics which should be treated in these workshops and invite you to send us all suggestions you might have. Companies accepting to host one of these workshops are very welcome to contact us or the Executive Committee, to learn more about the envisaged concept and practical prerequisites. We are convinced that with your input and support we should be able to carry out the process of such a workshop in less than one year.

We promise to keep you informed via the ESTP newsletter and are looking forward to your suggestions.

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## ANNOUNCEMENT

### XXII Classic Examples in Toxicologic Pathology

**February 20&21, 2015**

RITA is an industry sponsored project for generation and maintenance of a historical database for control animals from rodent carcinogenicity studies. Recently, the group has expanded its focus from conventional carcinogenicity studies in rats and mice to carcinogenicity studies in hamsters and short-term carcinogenicity studies in transgenic ras H2 mice.

**Panel meetings in 2015:** Beginning with the year 2015, panel meetings will start on Monday at 1:00 PM. and will last until Wednesday noon. An exception will be the first panel meeting next year, which will be held from Wednesday to Friday, February 18–20. This will give participants the opportunity to attend the seminar “Classic Examples”, which will begin subsequently, on Friday, February 20, 1:00 PM. Due to the prolongation of panel meetings from 1 ½ days to two days it was possible to reduce the annual number of meetings from five to four. The schedule of meetings in 2015 is:

February 18 - 20  
May 18 - 20  
September 07 - 09  
November 30 – December 02

The ‘microscope panel’ meetings of the RITA group are open to guests from regulatory agencies, non-RITA companies, contract laboratories and universities. The number of guests is limited to three, for organisational reasons. Guests will be charged 50 € covering lunches and beverages and must contact the organizer (Dr. Rupert Kellner, Tel.: +49 511 5350 106; e-mail: [rita.panel@item.fraunhofer.de](mailto:rita.panel@item.fraunhofer.de)) 4 weeks in advance of a meeting.

**The current status of the database:** The RITA project is currently running in its 10<sup>th</sup> 3-year contract period. Companies participating in the RITA project are: AbbVie, Amgen, AstraZeneca, BASF SE, Bayer AG, Boehringer Ingelheim Pharma GmbH & Co. KG, F. Hoffmann-La Roche Ltd., Merck-Serono, Novartis Pharma AG, Novo Nordisk A/S, Sanofi-Aventis, Syngenta and Takeda Pharmaceutical Company Ltd.

Currently, the database contains 177 rat studies with more than 28,000 primary tumors and almost 32,000 preneoplastic lesions. The 85 conventional mouse studies in the database include about 7,500 primary tumors and 4,500 preneoplastic lesions. It is planned to increase the number of studies in transgenic ras H2 mice (with data from negative and positive control groups) from currently 6 to at least 10 by the end of the next year.

**For more information see:**

<http://reni.item.fraunhofer.de/reni/public/rita/index.php>

With regards,

Thomas Nolte (Chair) & Matthias Rinke (Co-chair)

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For many of us, the “Classic Examples” in Hannover are an important date in the calendar: it is the first important scientific meeting and the first occasion in the year to meet colleagues and friends. Our next year’s seminar will take place on **Friday, February 20 and 21**. As in the past, it will be jointly organized by the University of Veterinary Medicine in Hannover and the ESTP. It will take place at the Department of Pathology of the University of Veterinary Medicine in Hannover, Bünteweg 17.

Examples of toxicologic pathology will be presented and discussed by the participants. Sixty slide sets will be provided for in maximum 120 participants. However, in some cases and for some lesions the preparation of additional slides may not be possible. In order not to miss such cases, we look for a solution to offer scanned slides to the participants.

Our preliminary program includes presentations on the following topics:

Taxoids  
Lipidated protein  
Pathophysiology of iron homeostasis  
BACE1 / BACE2-inhibitors  
Antisense oligonucleotides  
Inhibition of sphingosine 1-phosphate lyase  
Liver spheroids  
Vehicle-induced lesions  
PDK1-inhibitors

All ESTP members will be informed by e-mail when the seminar is open for registration.

The organizers:

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