

ESTP Newsletter 2015 (1)



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President's column



Dear ESTP members,

Welcome to the first newsletter of 2015! I hope that you had restful vacations in December and are now ready for another busy and challenging year in toxicologic pathology. The ESTP Executive Committee (EC) already has a number of new and exciting initiatives which it is involved in this year. The first of these, and one which the full membership has already been emailed about, is the response to the recently published OECD document on peer review. One of our eagle-eyed members had already spotted that since our latest discussions, the OECD had updated the guidance document from 26 Sept 2014 to 15 Dec 2014. This was merely a page change. However, it does highlight that we need to be on the alert for changes in regulations which affect our daily work. Regarding the whole topic of OECD peer review, the STP's Scientific and Regulatory Policy Committee (SRPC) is driving this initiative through strong interaction with the global communities, including our Japanese colleagues. There is a target to be in a position to share the SRPC's first draft manuscript within the next

few weeks. There will be a two week input period, and it was also felt that endorsement by the global STPs of the final version of the manuscript would strengthen the impact of this manuscript which will be submitted to *Toxicologic Pathology*. A formal endorsement should certainly have a greater impact than a simple global input. The membership will be updated as this process progresses.

I am also pleased to report that preparations for our first "Adversity" Workshop are well underway. This two day meeting will be held between the 8th and 9th June 2015 at Sanofi, Paris and is entitled "The ESTP International Expert Workshop on the use of the term 'adverse' ". Within the organizing team, Xavier Palazzi is the host and local organizer and Gabriele Pohlmeier-Esch and Wolfgang Kaufmann wrote an article on this in last year's newsletter and please read the accompanying article in this newsletter. Letters of invitation have now been sent out to representatives of the pharmaceutical and chemical industry and regulatory authorities and we look forward to having expert discussion on this important topic, with a view to producing a consensus report in a peer reviewed international journal which represents the views of toxicologists, pathologists, regulators and those involved in Phase 1 trials.

We are additionally excited about another new initiative in providing continuous pathology education to our members and beyond. This is our first ESTP Pathology 2.0 group's webinar on tissue section-based investigative technologies. There will be a series of four webinars this year with the first being focused on immunohistochemistry and its application in toxicologic pathology. This will take place on the 24th February and I would encourage you to check out our website for further information regarding registration. Special thanks must go to Franck Chanut as Chair of the Pathology 2.0 committee and Silvia Guionaud for organising this.

One aspect of our work that is continually evolving in discussions is the use of digital pathology imaging in toxicologic pathology. This was one of the topics at the last International STP Leaders' Meeting in December and it was interesting to learn that the diagnostic pathology field (both in human medicine and veterinary medicine) is ahead of the toxicologic pathology field in that regard. This is understandable as diagnostic pathology is not subject to the most stringent of regulations on data output. However, the use of this technology and the setting up of guidelines for validation in its usage which will satisfy the regulatory authorities is an area where the diagnosticians and toxicologic pathologists can work together. The quality and resolution of image together with the speed of scanning produced by the latest high speed scanners is truly impressive. This technology was demonstrated recently at the London Vet Show (see photo) where the quality imagery and benefits of rapid second opinions, live discussion with other pathologists, and use for educational material, was readily demonstrable. With a forthcoming review article by some US toxicologic pathologists, which is a compilation of at least 8 posters presented by the USA NTP (National Toxicology Program), I am certain that this is one area which will no doubt be heavily discussed and developed within the next few years.



Finally, I would encourage you to inform us of any of your ideas or thoughts on ways in which the Society can operate better for you. We are always keen to receive feedback. I look forward to meeting with some of you face to face at the Classic Examples in Toxicologic Pathology at Hannover in February.

Thank you for your membership and support.

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International Harmonization of Nomenclature and Diagnostic Criteria (INHAND): Progress to Date and Future Plans

Standardization of microscopic pathology nomenclature and diagnostic criteria, especially for rats and mice, has been under discussion for many years by pathologists in the profession of toxicologic pathology. In 2005, the Society of Toxicologic Pathology (STP) and European Society of Toxicologic Pathology (ESTP), along with Registry of Industrial Toxicology Animal-data (RITA), established a collaborative process to review, update, and harmonize existing nomenclature documents and databases. The British Society of Toxicologic Pathology (BSTP) and the Japanese Society of Toxicologic Pathology (JSTP) joined the project in 2006, making this a genuinely global initiative. The result of these discussions was the INHAND Proposal (International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice). A Global Editorial Steering Committee (GESC) manages the overall objectives of the project, and Working Groups (WG) formulate the terminology proposals for each organ system¹. Both the GESC and the WGs are composed of experts from the North American, British and European and Japanese Societies of Toxicologic Pathology.

Noteworthy headway has been made with 9 systems to date. Rodent Respiratory, Hepatobiliary, Urinary, Central/Peripheral Nervous Systems, Male Reproductive and Mammary, Zymbal's, Clitoral and Preputial Glands have been published in *Toxicologic Pathology*, official journal of the STP and the BSTP. The Integument and Soft Tissue Systems and Female Reproductive System have been published in the *Journal of Toxicologic Pathology*, official journal of the JSTP. These manuscripts can be found as supplements in the respective journals and on the goRENI (global online Registry Nomenclature Information) System web site – www.goreni.org - with member access for scientists working in the field of toxicologic pathology, members of any society of toxicologic pathology or of a regulatory agency. INHAND guides provide diagnostic criteria and guidelines and preferred terminology for recording lesions observed in rodent toxicity and carcinogenicity studies. The guides also provide illustrative photomicrographs of lesions and information regarding pathogenesis, along with germane references. The goRENI web site also provides convenient, online, interactive access to the diagnostic criteria and images for each individual diagnosis that many pathologists find useful and refer to while conducting their microscopic evaluations.

INHAND and GESC will continue current WGs until publication of all systems is complete. The remaining rodent systems include Digestive, Cardiovascular,

Skeletal, Endocrine, Special Senses and Lymphoid/Hematopoietic. In order to establish the format and style that would be suitable for the content of these nomenclature guides, the STP supported the publication of the first several systems in Toxicologic Pathology. Working closely with scientific and technical colleagues from Toxicologic Pathology, the editorial and scientific staff of the Journal of Toxicologic Pathology adapted the publication style to their journal, so that the appearance of all INHAND supplements will remain uniform, regardless of the journal in which they are published. As new organ systems become available for publication, the GESC will coordinate with the editorial staff of *Toxicologic Pathology* and the *Journal of Toxicologic Pathology* to ensure equitable distribution of supplement publications and in the most effective and cost-efficient manner. Whether systems will be published separately or bundled together will depend largely on the size of the documents.

Non-Rodent Terminology

In addition to terminology for rodents, a new directive for separate committees to develop species-specific terminology has been established under GESC – dog, monkey, rabbit and minipig. Committees are reviewing the rodent nomenclature as the starting point and then providing a manuscript on terminology that is in common use in each species, terminology that is unique for each species as well as rodent terminology not appropriate for use in non-rodent species. This information would be posted on goRENI. Publication as an article or supplement will be determined on a case-by-case basis.

Relationship between INHAND and SEND

During 2012, INHAND GESC representatives attended meetings with representatives of the FDA Center for Drug Evaluation and Research (CDER), Clinical Data Interchange Standards Consortium (CDISC), and the National Cancer Institute (NCI) Enterprise Vocabulary Services (EVS) to initiate integration of INHAND terminology as the preferred terminology for SEND (Standard for Exchange of Nonclinical Data). SEND is a formal mechanism for submitting data from non-clinical studies to the FDA electronically and in a standardized format. INHAND GESC assists the SEND Controlled Terminology (CT) committee in providing definitions for base processes and modifiers associated with the INHAND published terminology. INHAND ad hoc members of the SEND CT committee will participate in this endeavour and take issues to the full GESC and/or appropriate OWG for resolution. The GESC may also call on experts in the field to assist in any aspect of their role as a ‘Scientific Advisory Board’. The interest in utilizing the INHAND nomenclature, based on input from industry and government toxicologists as well as information technology specialists, signifies the potential for wide acceptance of this nomenclature².

GESC will become a permanent standing committee of the various Societies of Toxicologic Pathology with a defined appointment and term of members and establishment of several new roles, due to the expectation for ongoing interactions with the SEND project and future needs to serve in an advisory role. GESC will act as a clearinghouse for comments and requests for updates to the INHAND terminology from the SEND CT committee as well as from the memberships of each Society.

INHAND as an ongoing process

Although the published INHAND nomenclature for each organ system is expected to be very comprehensive, it is recognized that additional lesions may need to be included, omissions rectified or inaccuracies corrected as they become apparent. To address this, a formal change control process was implemented in 2013 and is available on www.goreni.org and each Society website. Society members are encouraged to submit suggestions for changes to the nomenclature systems and provide justifications for such changes through this mechanism. GESC will continue to interface with goRENI and editorial staff at the journals so that the basic structure for future publications is maintained.

The GESC and STP, BSTP, ESTP and JSTP leadership greatly appreciate the efforts of all of those serving on the WGs and the newly-formed non-rodent working groups, and look forward to working with the global toxicologic pathology community as additional systems are drafted, reviewed, and completed. The international scope and review of the INHAND documents will provide a strong framework for use by pathologists and regulatory agencies that are engaged in the safety assessment of drugs, biologics, and chemicals.

References

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2. Keenan CM and Goodman DG. Regulatory Forum Commentary*: Through the Looking Glass—SENDing the Pathology Data We Have INHAND. *Toxicol Pathol.* 42: 807-810. 2014.

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Update: ESTP International Expert Workshop on the general definition and use of "adversity"

Dear ESTP members,

As presented at the Annual General Assembly 2014 in Berlin, our Society has committed to organize a new series of ESTP International Expert Workshops, in order to review, define and put into practical perspectives the organ-specific notion of adversity in toxicity studies. The topic of the first workshop was endorsed by the Executive Board and will consist in reviewing the numerous definitions already proposed for "adversity", adding in the perspective of regulators, toxicologists and clinicians from the pharmaceutical and chemical industry, in order to "set the rules" for the following workshops.

We are grateful to Sanofi, Paris, and to Xavier Palazzi who kindly offered to host this first workshop, the face-to-face final discussion of which will take place on 8th-9th June, 2015. Based on suggestions from the membership, the list of participants is almost complete and will involve internationally recognized experts from Europe, the USA and Japan as well as a number of volunteering ESTP members. We plan to structure the initial working phase of this initiative by attributing a topic to each of the participants. These topics (or provocative statements) will be agreed upon during a first teleconference towards the end of February.

Our next challenge will be a technical one. We have the objective to allow passive and/or active participation of a maximum number of ESTP members in the process. To achieve this we plan to record the face-to-face discussions between experts, to extract the most important take home messages and to make this video available on the ESTP website. In addition, we are currently looking into the possibility of accepting a limited number of scientists physically at the meeting. We will keep you informed about the practical modalities to join this audience. Therefore, please mark your calendars for the 8th/9th June!

In the meantime, please feel invited to contact us any time in case you have suggestions or wish to receive further information.

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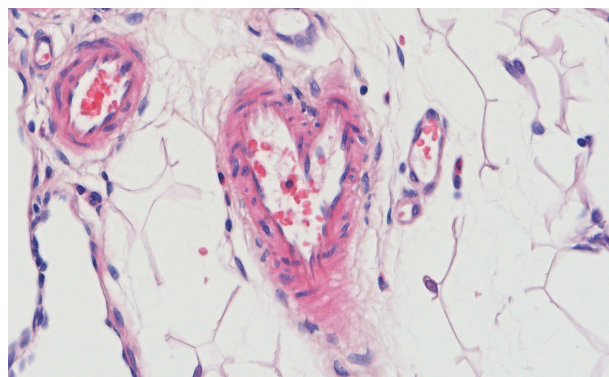
Meeting Calendar on the ESTP Homepage

On the ESTP Website, we list all meetings which are of interest for our profession and update it regularly. Our calendar includes a unique user-friendly searchable facility to enable the finding of a meeting by location, organization, date and keywords.

<http://www.eurotoxpath.org/calendar/index.php>

If you know any upcoming meeting, conference or workshop which you recommend to be listed on the calendar, please send the information to:

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Courtesy of Annabelle Heier