

ESTP Newsletter 2019 (3)



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President's Column

Dear ESTP members,

The year is coming to its end, and it's time to also look back after a busy year and review what has been accomplished. My highlight as it was in the previous years was our annual ESTP congress in Cologne. The congress took place in parallel with the annual congress of the European Society of Teratology. It was a great success and the hot topic, "Digitalization meets Pathology", attracted over 200 participants, which is a record for the ESTP! On behalf of the ESTP members and Executive Committee, I would like to take the opportunity to thank the entire Scientific Organizing Committee chaired by Sibylle Gröters and Björn Jacobsen. Moreover, I would like to thank the IATP for organizing a satellite symposium, our excellent speakers and finally all participants, who created a fantastic atmosphere for scientific exchange and social networking. The 7th ESTP International Expert Workshop "Towards Regulatory Acceptance of Digital Toxicologic Pathology" organized by Vanessa Schumacher, Erio Barale, Xavier Palazzi and Pierluigi Fant, was held directly after the congress. Expert discussions and questions from the audience were interposed between presentations given by the invited experts. The aim is to publish the results in the Toxicology Pathology special issue on Digital Pathology, Tissue Image Analysis, Artificial Intelligence, and Machine Learning.

The Annual General Assembly took place on September 19, 2020 before the lunch break and it was very well attended. For those, who had no opportunity to join the AGM, all information will be available on the ESTP homepage soon and include the annual reports of the executive committee members, councilors and working groups. Solution Office headed by Pia Schröder and Kay Groothoff was official thanked since it was their last conference that they organized for the ESTP.

I am delighted that the committee Pathology 2.0 has resumed its work after some inactive months. Thereby I would like to thank you Thomas Lemarchand, departing Chair, and welcome Vanessa Schumacher as the new Chair of Pathology 2.0. At the moment, the committee on Clinical Pathology is inactive and without any chair, since Aïda Diaz-Bayon has resigned: thank you Aïda! I would like to encourage members who wish to work on clinical pathology to contact our Secretary Gabriele Pohlmeier-Esch or myself. In this place, I would also like to remind you that we are calling for candidates for the ESTP Secretary position to the end of this year, in order to ensure a smooth transition by gradually "introducing" Gabi's successor. The next periodic electronic elections for the ESTP Executive Committee will take place between May and July, 2020. As usual, we will call for candidates for all other EC positions in the early spring.

At the Global Toxicologic Pathology President Group Meeting in Cologne, Charlotte Keenan gave an update on the progress of The International Harmonization of Nomenclature and Diagnostic Criteria (INHAND) efforts. The GESC recently completed a comprehensive review across all rodent organ systems to identify inconsistencies, and updated terminology for better consistency. This information was shared with society members and is also on goRENI. The mini-pig and rabbit are out for membership comments, and you have recently received the rodent hematology system, which was published as a normal issue of Toxicological Pathology in order to reduce the costs. Due to the scope of work left for the non-rodents, the support for the goRENI contract has been extended for 2020. The status of the comments to the FDA Draft Guidance on Peer Review was discussed. The STPs official response was sent by September 16, and the ESTP Committee for Scientific Standards has collected comments from our ESTP members and participating institutions in order to provide a response to the FDA, which you received in October. Another topic was predatory journals and conferences, with the intent to ask

Susann Elmore if it would be possible to have this topic addressed in Toxicological Pathology.

I would like to highlight some activities which took place during the summer and some future activities and challenges. Since 2015, the ESTP had sent a representative to the ECV/ESVP Summer School for introducing and promoting our discipline to young ECV/ESVP trainees, with the goal to attract some new toxicological pathologists. This year, Giovanni Pellegrini gave a presentation on career possibilities in Tox Path at the Summer School, held between 15th and 26th July in Alfara del Patriarca, Valencia, Spain. The ESTP also sponsored the travel costs of one lecturer, as well as one key note lecture at the joint ESVP-ECVP-Veterinary Clinical Pathology congress, September 25 – 28, 2019, in Burger's Zoo in Arnhem in The Netherlands. Jürgen Funk gave a presentation entitled "Immune-complex glomerulonephritis in monkeys after treatment with biologics – Case example and career pathways" which was very well received. I also attended the ESTP Board meeting together with representatives from the ECV/ESVP for joint discussions on how the college and societies can collaborate in the future, with special emphasis on our joint cutting edge pathology (CEP) meeting in 2020. Finally, I met the local organizer of the CEP meeting, Prof. Enrico Bollo, and representatives of Pauwels Professional Congress Organizer, who will organize our congresses from 2021 and onwards. Pauwels organized the congress in Arnhem very professionally. I am confident that we will have a good collaboration with them in the future.

Please do not hesitate to contact me. I highly value feedback from our members and would welcome suggestions and ideas for future activities from the membership. I would also gladly answer any questions. Finally, thank you to all of the ESTP Executive Committee Members, for the giving of their "spare" time and many hours of work to the organization. I look forward to meeting some of you again at the Classic Examples in Hannover, February 21-22, 2020, and if not there, then at the CEP Meeting in Torino, August 26-29, 2020 in Italy!

Finally, I would like to encourage everyone to volunteer and to continue to support our Society.



I wish you a Happy Holiday Session and a Happy New Year.

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ESTP Response to FDA Draft Guidance on Pathology Peer Review in Nonclinical Toxicology Studies

On August 01, 2019, the FDA Office of Study Integrity and Surveillance (OSIS) published a Draft Guidance on "*Pathology Peer review in Nonclinical Toxicology Studies: Questions and Answers, Guidance for Industry*" in the Federal Register for public comment. This information was immediately forwarded by the STP Scientific Regulatory Policy committee (SRPC Committee) and ESTP liaison, so that the Draft guidance could be shared swiftly with the ESTP Executive committee and ESTP Committee of Scientific Standards (CSS) for review. In addition, a communication was sent to the ESTP membership within a couple of days to call for comments within the rather short comment period of 2 months. In parallel, the ESTP CSS coordinated the preparation of an ESTP response to the FDA. Several comments were received from individual ESTP members and industry pathology groups. Most of the latter were provided to the FDA separately. Due to the short review period in the middle of the main summer vacation period, the ESTP CSS formally requested an extension of the comment period, which was informally granted via e-mail communications with FDA representatives. Finally, on October 18, the ESTP CSS and Executive committee submitted a very detailed response in tabulated form, addressing all paragraphs by providing respective context and alternative wording, if deemed required. The official response has been also shared with ESTP members via e-mail, is posted on the ESTP webpage, and has been shared with sister and partner societies.

The current FDA draft guidance is vividly discussed in the community of Toxicologic pathologists, as it raises a number of new requirements, which are intended to protect data integrity. In 2014, the OECD Guidance No. 16 on GLP Requirements for Peer Review of Histopathology has had substantial consequences on the Pathology peer review process in industry by adding formal aspects to ensure transparency of the process. The ESTP and its membership has been actively involved in correspondence with the OECD Working group on Peer review during the establishment of the first OECD Advisory document No.16 between 2010 and 2014, and has also contributed to STP expert working groups, publications and commentaries on the scientific and compliance aspects of peer review (Fikes *et al.*, 2015; Morton *et al.*, 2010). Those publications were a product of

global collaborations with other international societies of Toxicologic pathology, including the ESTP.

Again this time, the close and constructive collaboration with sister and partner societies in Toxicologic Pathology was very helpful to be able to react in a timely and impactful manner on this key FDA Draft guidance in the field of Toxicologic Pathology.

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Chair of the ESTP CSS

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Fikes JD, Patrick DJ*, Francke S*, Frazier KS, Reindel JF, Romeike A*#, Spaet RH*, Tomlinson L and K Schafer* (2015). Review of the Organisation for Economic Co-operation and Development (OECD) Guidance on the GLP Requirements for Peer Review of Histopathology. *Tox Path*, vol. 43, 7: pp. 907-914.

Morton D, Sellers RS, Barale-Thomas E*#, Bolon B*, George C*#, Hardisty JF*, Irizarry, McKay JS*#, Odin M, and M Teranishi (2010). Recommendations for Pathology Peer Review, *Tox Path* 38: 1118-1127.

*ESTP member

#Europe based

ANNOUNCEMENT

Classical Examples in Toxicologic Pathology

XXVII

February 21-22, 2020 – Hannover, Germany

The next Classical Examples in Toxicologic Pathology will take place on February 21 and 22 at the University of Veterinary Medicine in Hannover. Please find the program below:

- Drug-induced small intestine pathology. Speaker: Marielle Odin.
- Liver findings with gene therapy. Speaker: Ingrid Pardo.
- Drug-induced neutropenia in dogs. Speaker: Michael Winter.
- Device-induced growth plate lesions. Speaker: Dirk Nehrbass.
- Polycystic lesions in SD rats. Speakers: Silke Treumann, Heike Marxfeld.
- Genetically induced inner ear lesions. Speaker: Andreas Popp.
- Mc1-1 inhibitors. Speaker: Florian Colbatzky.
- mTOR inhibitor in combination therapy – kidney lesions. Speaker: Johannes Zellmer, Hsi-Yu Yen.
- Monovalent FGFR1 antagonist. Speaker: Anja Knippel.
- Mutation-specific drugs. Speaker: Florian Colbatzky.

The seminar will be held in English. Examples of toxicologic pathology will be presented and discussed by participants, viewing slides with the induced lesions under individual microscopes or as electronic slides. The electronic slides will be accessible for registrants approximately 2 weeks in advance of the seminar, during the seminar, and approximately 4 weeks thereafter.

Please register as soon as possible, at the latest by January 31, 2020, via the ESTP homepage

http://www.eurotoxpath.org/meetings/index.php?id=class_exam2020.

On behalf of the organizers,

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Some Thoughts of a Retiree from Tox Path

After working for industry in toxicologic pathology for many years, some of you might think that it is time to just relax and reflect on a successful career. Some of you in this position might have retired voluntarily, while others may have been forced into early retirement for economical or even “political” reasons. After retirement, many colleagues remain active in the community, while others just vanish. I think it is the absolute right of everybody to do so as he or she likes, and there is no good or bad.

Several of you may recall me as your ESTP Treasurer for about a decade, always asking for your willingness to support our Society (including your money!). Ultimately, I stepped back from this position, not due to a lack of time, but because I felt it necessary that the treasurer should be an active part of the community and to be in the middle of the daily business. However, this did not mean that I would withdraw my interest in our Society’s daily life. Thus, I was amazed (and a bit honored) when our Councilor for the Newsletter asked me if I would be willing to write a few sentences about my experiences as a retiree.

Okay, here we go: Three years ago, I retired after 30 years of service in toxicologic pathology, which included roles as study pathologist and group lead. During my career, I always had the idea to enjoy my time after retirement, after the routine of getting up early, being at work on time, frequently working overtime and even on weekends. And I did not want to wait before I was too old to enjoy the advantages of being independent.

The key word here is “enjoy”. I always enjoyed working in the field of veterinary and toxicologic pathology. I became a veterinarian because I loved animals (especially “wild” ones) and science at the same time. Pathology became not only a field of interest but a profession to me.

No other discipline seemed to provide me with so much new and concurrently exciting experiences, and to encourage me to dive deeper and deeper into the scientific literature... and often to find that frequently there were colleagues who had the same thoughts decades ago.

When the time for my retirement came closer, I was wondering what I could do to maintain my interest in veterinary pathology and - at the same time - to not waste my knowledge in the field that I had gained over the years. And all that without being dependent on timelines or other professional pressures. Therefore, I decided to support an environmental conservation program focused on otters. This was an interest that began around the time when I started to study veterinary medicine. Already at that time I liked the approach of the *Aktion Fischotterschutz e.V.*: First we need a healthy environment before we can re-introduce an endangered species back to the wilderness. To make a long story short: I paid my annual dues, participated now and then at membership meetings and finally realized that there is an enormous lack of facts on the health status in this endangered species. Yes, occasionally Eurasian otters are necropsied in the institutions for veterinary pathology, but then they are just one case among many others, and not much experience is available to assess the results received in a broader pathological context.

In contrast to toxicologic pathology, in diagnostic situations such as these there are no concurrent controls or even historical control data available. Thus, I thought it useful to review cases from the archives to gain data for a more systematic overview on common background findings of otters. And I was lucky to have received this chance in my "old" institute at the Veterinary University in Hannover (Thank you WB). This way, I have learned amazing things about periportal liver fibrosis and bile duct proliferation, the presence of mucinous cystic hyperplasia of the gall bladder and urolithiasis in the polyreniculated kidney of otters. Questions come up like: are hepatocellular foci comparable to preneoplastic lesions in rodents? And, is there a need for a commonly used terminology in veterinary and toxicologic pathology? What can we learn from each other in these two similar disciplines? And yes, I was confronted with a lot of hyperemia and autolysis.

Retrospective histopathology was only one side of this shiny coin. Performing necropsies on about 20 otters in a team of fully enthusiastic young veterinary graduates and engaged technical staff was my recent highlight in this fantastic project. Of course, it is depressing to see how many otters become victims of road accidents when they cross roads on their long tours to find suitable habitats, food or partners. But being among these young scientists in the Institute of Aquatic and Terrestrial Animal Sciences in Büsum was just amazing and made me feel quite young again. Curiosity paired with excitement has embraced me, and the experience that even long time freezing does not

destroy structures (too much at least, especially if you carefully warm up the carcasses again), has provided me with the wonderful picture of an apocrine and partly holocrine sebaceous scent gland nicer than that found in any histology text book.

Thank you for allowing me this update. I just wanted to let you know that, despite many days of long hours and hard work, for me the unique opportunities and diversity of experience provided by our profession is a gift that we can all share.

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**17th ESTP Congress and 17th ESTP
International Expert Workshop "Towards
regulatory acceptance of digital toxicologic
pathology"
September 17-21, 2019 – Cologne, Germany**



The 17th European Congress of Toxicologic Pathology in Cologne had a theme of Digitization meets Pathology. A topic of great interest for me. The first day provided a good overview of the digital imaging concerns. Ranging from digitization of glass slides to whole slide images (WSI), an overview of artificial intelligence terminology and disciplines underlying algorithm authoring, to workflow concepts regarding the incorporation of WSI into the daily life of a pathologist. The day ended with a delightful welcome reception in which colleagues interacted in a friendly, interactive time to renew old acquaintances and build new networks.

The subsequent sessions build upon the foundation of the first day with specific examples of image analysis using artificial intelligence algorithms. Other presentations expounded the future potential of AI assisted image analysis and how it would augment pathologist daily activities. Allowing them to minimize the daily mundane activities to investigate deeper scientific endeavors. This was reinforced with examples of institutions which have currently adopted digital workflows. The meeting then

closed with a series of informative case presentations. One of the high points of the week was the dinner in the Wartesaal, which was held in the renovated “old train stations”. The facility was beautiful and the group interactions even better.

The post meeting workshop Towards Regulatory Acceptance of Digital Toxicologic Pathology was very insightful as well. A frank discussion on the use of WSI in daily workflows from a regulator perspective was discussed and many thought provoking points were discussed. One of my high points of this meeting was seeing the congruency between regulatory representatives for the use of WSI for peer review and primary evaluation on GLP studies.

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CALL FOR VOLUNTEERS

News from the *ToxPath* Journal: next journal Editor-in-Chief.

Dear ESTP members,

You may have seen the recent advertisement “Opportunity is knocking: Are you the next editor of *Toxicologic Pathology*?” The term of Susan A. Elmore (current Editor) ends on December 31, 2020, so the search for the next Editor-in-Chief has begun. To ensure a smooth transition, the goal is to have a successor appointed by July. Application review will begin on January 31, 2020. For more information on the desired qualifications, job description and application submission, see <https://www.toxpath.org/membersonly/docs/TPX-Journal-Editor-in-Chief.pdf>.

Toxicologic Pathology is the official journal of the Society of Toxicologic Pathology (STP), European Society of Toxicologic Pathology (ESTP), and British Society of Toxicological Pathologists (BSTP). This journal is a premier publication for communicating original research findings, comprehensive reviews, and current practice recommendations in toxicologic pathology.

Best regards,
Emmanuelle

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