



September 19, 2005

To:
The Society of Toxicologic Pathology (STP)

Dr. Nancy Everds, President
Dr. Colin Rousseaux, Past-President
Dr. Dan Morton, Chairman of the "Strategic and Regulatory Policy Committee"

Re: Your draft proposal: *"Revision of Standardized Nomenclature for Lesions in the Rat and Mouse"*

Dear Colleagues,

The chairmen of the RITA group, Thomas Nolte and Matthias Rinke, both members of our society, brought your initiative to our attention. We, as the ESTP, appreciate and support your initiative very much and want to offer an active co-operation in the revision process that should result in a standardized nomenclature for proliferative and non-proliferative lesions of worldwide acceptance.

In order to reach the ambitious goal of an international, global acceptance of a revised nomenclature as "reference guides", your initiative should encompass views borne by all major societies of toxicologic pathology. In this way, it will be possible to gain the knowledge of the best international experts for active participation and to also include regional specificities.

Regarding the procedure, the ESTP would like to make some additional suggestions from our European point of view:

As outlined in your draft proposal, the implementation of **organ working groups** is the central part of this process. Preparation of new manuscripts and revisions of existing manuscripts should follow a mutually agreed structure and layout. This frame should be discussed and defined by an **international editorial board**, which needs to be implemented first.

The entire field outlined in your draft proposal will include a huge amount of work, even if divided by organ systems. Therefore, the ESTP suggests subdividing the organ systems into "working packages":

1. non-proliferative lesions (including clinical pathology where appropriate) in rats
2. non-proliferative lesions (including clinical pathology where appropriate) in mice
3. proliferative lesions in rats
4. proliferative lesions in mice

In the past 15 years, STP colleagues were leading in the field of establishing diagnostic criteria for **non-proliferative lesions** and therefore we feel that the STP should remain the driving force for this part. Of course, the ESTP will cooperate and provide input in order to support you in this attempt.

In Europe, toxicologic pathologists have put much effort into **proliferative lesions**, particularly triggered by the RITA project. Due to the involvement of many ESTP members in the RITA project, the ESTP sees its main focus of competence in the further work on proliferative lesions. Among the proliferative lesions, the ESTP and the RITA group recognizes in particular a need to revise the **rat**, as:

1. two different nomenclature systems exist (WHO / IARC and STP)
2. the publication of the first WHO fascicles dates back to 1992, that of the STP back to 1990.
3. an international panel of experts, consisting of STP, RITA and NACAD members, has agreed upon a harmonized nomenclature of proliferative lesions in rats (2000, see http://reni.item.fraunhofer.de/reni/rat_nomenclature/index.htm). However, it has never been published in conjunction with the respective diagnostic criteria

For proliferative lesions in **mice**, there is, from the ESTP point of view, currently only a minor need for updates. This is because the nomenclature and diagnostic criteria were published in 2001 in a joint effort by the STP and the RITA group, under the auspices of WHO/IARC.

The ESTP therefore strongly suggests, that for proliferative lesions the ESTP and the RITA group overtake the initiative for the following reasons:

1. RITA has more than 17 years experience in the field of nomenclature and diagnostic criteria.
2. RITA has already identified colleagues with special experience and interest in certain organ systems. They act as "compilers" and are responsible for the update of manuscripts. Update of nomenclature and diagnostic criteria is done continuously, depending on the demands by new knowledge.

3. Updates are performed in the electronic version of the published WHO / IARC nomenclature, the WebRENI system.
4. During recent years, RITA has continuously collected photographs on representative and borderline cases; altogether, more than 3,500 high resolution digital images are now available.
5. Colleagues from the RITA group have access to more than 47,000 peer-reviewed hyperplastic and neoplastic lesions in rats and mice, stored in the database.
6. With the merger of RITA and NACAD, the RITA project now involves experts from Europe and the US.

The ESTP is very grateful that the RITA group is willing to provide the available material and knowledge to form the basis for the revised and internationally accepted nomenclature and diagnostic criteria. Fraunhofer ITEM is currently evaluating technical concepts and clarifying legal (copyright) aspects in order to make the WebRENI System available as a platform for a global discussion of draft manuscripts. The ESTP strongly suggests accepting this generous offer from the RITA group and Fraunhofer ITEM.

With regard to the sequence of organ systems to be drafted, we suggest to link them to the main topics (regarding the organ system) of future STP and ESTP annual congresses. Publication of the revised manuscripts should be broadened to include Experimental and Toxicological Pathology, the Journal of the ESTP, and the Japanese Tox Path Journal as well.

We support beginning with (1) the immune system and (2) the respiratory system.

We, as ESTP, feel this kind of international co-operation is a first concrete step for the benefit of all toxicologic pathologists in the follow-up of diverse verbal statements and discussion rounds in the past. It is the right track and one which we all want to follow. It will also strengthen our profession and scientific statements in the field of product safety.

We are looking forward to an exciting and productive co-operation!

With kind regards,

Wolfgang Kaufmann
ESTP Chairman