INHAND: <u>International Harmonization of</u> <u>Nomenclature and Diagnostic Criteria</u> for Lesions in Rats and Mice - An Update

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Background:

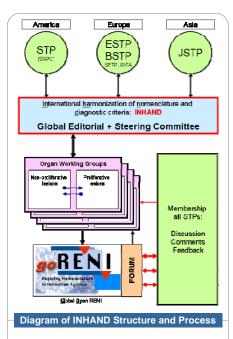
Harmonization of nomenclature and diagnostic criteria in toxicologic pathology, especially for rats and mice, has been a goal of pathologists working in the profession for many years. In the latter part of the twentieth century, several initiatives were undertaken by the STP in the United States and by the RITA data base group (Registry of Industrial Toxicology Animal-data) in Europe. Their efforts resulted in a number of internationally recognized publications: SSNDC: Guides for Toxicologic Pathology and the WHO/IARC International Classification of Rodent Tumors. Beginning in 2005, the STP and European Society of Toxicologic Pathology (ESTP), in conjunction with RITA, developed a collaborative process to review, update, and harmonize existing nomenclature documents and databases. In 2006, the British Society of Toxicologic Pathology (BSTP) and the Japanese Society of Toxicologic Pathology (JSTP) joined the initiative, so that the project has become truly global.

Objectives:

• Produce publications for each organ system that provide a standardized nomenclature and differential diagnosis for classifying microscopic lesions observed in laboratory rats and mice in toxicity and carcinogenicity studies.

Structure

- Global Executive Steering Committee (GESC) with representation from major societies of toxicologic pathology
- 15 organ system working groups (OWG) defined by GESC
- Each group is composed of expert toxicologic pathologists from each of the participating societies and is responsible for developing preferred nomenclature and diagnostic criteria
- Terminology based on
 - SSNDC for non-proliferative
 - RITA/WHO/IARC and
 - Terminology of "International Harmonization of Rat Nomenclature" for proliferative lesions
- Diagnoses discussed by OWG and may be extended/amended



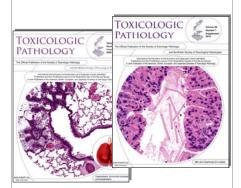
- OWG develop nomenclature primarily descriptive in nature and denote findings which can be documented from the review of routine histologic specimens
- Once the draft nomenclature has been developed, GESC completes an initial review, followed by a period during which all members of participating societies are requested to review the proposed nomenclature
- OWG then finalizes the nomenclature based on comments from the GESC and general membership.
- An important feature of INHAND is the use of the goRENI (global open Registry Nomenclature Information System, <u>www.goreni.org</u>) as a webbased platform to both review draft nomenclature and publish final nomenclature. Originally developed by RITA, goRENI provides access to members of all STPs as well as government regulators.

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goRENI (global open Registry Nomenclature Information System), www.goRENI.org Incorporating specific diagnostic entities such as an infectious disease or diagnoses that imply a process that cannot be ascertained from routine histologic specimens (e.g. Phospholipidosis) is not recommended

Completed Organ Systems:

- Respiratory System
- Hepatobiliary System



In progress:

- Urinary System (reviewed)
- Nervous System (under review)
- Mammary Gland and other (reviewed)
- Integument (draft)
- Soft Tissue (draft)
- Lymphoid and Hematopoietic System
- Male Reproductive System
- Female Reproductive System
- Digestive System
- Skeletal System
- Cardiovascular System
- Endocrine System
- Special Senses

References

Renne R, Brix A, Harkema J, Herbert R, Kittel B, Lewis D, March T, Nagano K, Pino M, Rittinghausen S, Rosenbruch M, Tellier P, Wohrmann T (2009) Proliferative and nonproliferative lesions of the rat and mouse respiratory tract. Toxicol Pathol. 37 (7 Supp)):5S-73S.

Thoolen B, Maronpot RR, Harada T, Nyska A, Rousseaux C, Nolte T, Malarkey DE, Kaufmann W, Küttler K, Deschl U, Nakae D, Gregson R, Vinlove MP, Brix AE, Singh B, Belpoggi F, Ward M (2010) Proliferative and nonproliferative lesions of the rat and mouse hepatobiliary system. Toxicol Pathol. 38(7 Suppl):5S-81S.

Vahle J, Bradley A, Harada T, Herbert R, Kaufmann W, Kellner R, Mann P, Pyrah I, Rittinghausen S, Tanaka T (2009) The international nomenclature project: an update. Toxicol Pathol. 37(5):694-7.

Acknowledgements

Executive councils and members of the societies of toxicologic pathology who have supported this effort with resources and contributions to development of the organ system manuscripts.