The following are recommendations for Organ System Working Groups to use as they conduct their work.

**Organ System Working Group (OWG) Membership Established by GESC**

Global Chair  
BSTP members (1-3)  
ESTP members (1-3)  
JSTP members (1-3)  
STP members (1-3)  
NTP member/liaison (if possible)  
GESC liaison

If appropriate, the global chair may recommend one or more members to ensure the right balance in terms of expertise (e.g. proliferative and non-proliferative). The chair should consult with their GESC liaison for approval of additional members.

**OWG Duties**

- Draft documents describing the preferred terminology and diagnostic criteria for the organ system under consideration, including representative illustrations.  
  - OWG should evaluate and consider previously available nomenclature resources (GoRENI, SSNDC) and appropriate literature. ([GoRENI at www.goreni.org](http://www.goreni.org); SSNDC at [www.toxpath.org](http://www.toxpath.org) – click on Publications and Links; Standardized Nomenclature: SSNDC Guides)

- Scope of work for each OWG will include nomenclature for:  
  - Proliferative and non-proliferative lesions for rat and mouse.  
  - Spontaneous as well as common chemically induced lesions  
  - For transgenic mice, lesions which occur in alternative carcinogenicity models may be incorporated. It is not expected that OWG will provide a comprehensive nomenclature for all transgenic models (e.g. a target specific knock out).  
  - Dog and monkey terminology is not within the current scope of the project

- Provide regular updates to the GESC through their GESC liaison.
- Ensure appropriate review and approval of draft manuscripts by GESC
- Seek broad input of the toxicologic pathology community on draft manuscripts
- Finalize manuscripts and compile into a format suitable for publication.
Initial Organizational Steps

- Global chair sends an introductory email to committee members
  - Confirm that all members are willing to participate
  - Explain the general goals of the group
  - Distribute appropriate background documents for review prior to initial teleconference.
    - INHAND Proposal
    - Relevant nomenclature documents for the organ system
      - WHO, SSNDC,
    - Instructions for accessing GoRENI
    - If available, examples of completed work from prior OWGs
  - Request that members indicate their preference for proliferative versus non-proliferative assignments or organ-specific assignments.

- Initial Teleconference
  - Contact Krystle Corelle at STP (kcorrell@toxpath.org) for assistance in organizing teleconferences.
  - Suggested topics for teleconference include
    - Determine OWG structure. It is suggested that each OWG have sub-teams that cover proliferative and non-proliferative lesions; however, OWG may decide on alternate ways to organize their activities
    - Determine initial roles and responsibilities such as:
      - Reviewing and organizing available references
      - Gathering representative images
      - Drafting sections of the manuscript
    - Establish draft timelines
      - Suggested timing includes generation of a draft manuscript within 6 months of the initial teleconference.
      - In determining timelines, consider the adequacy of current terminology (GoRENI, SSNDC) for your respective system as well as the availability of high-quality images to illustrate terminology.
    - Initiate discussions on what types of induced lesions are appropriate for the organ system being considered

Process, Structure, and Expectations for Standardized Nomenclature

- Standardized nomenclature should be constructed according to the principles explained in the INHAND proposal and summarized in Appendix B of this document.
- OWG should develop a preferred term as well as collect synonyms for each lesion under consideration. As much as possible, additional fields and modifiers should be uniform across organ systems. The scope of the project does NOT include creating guidance for severity grades.
- For proliferative lesions, the OWG should use the nomenclature listed on the goRENI website as an initial framework. If the OWG finds the proliferative nomenclature to be acceptable, it will approve this nomenclature, and it will
become the “official” INHAND nomenclature. If the OWG feels that modifications to the goRENI nomenclature are needed, the OWG will discuss the proposed modifications with the RITA group to reach agreement on a single proliferative document. For many OWGs, this process can be facilitated by OWG members who are also active participants in RITA. If the OWG does not contain active RITA members, the OWG chair should contact their GESC liaison to facilitate RITA input and approval.

- For non-proliferative lesions, the OWG will use the SSNDC guide (if available) as well as the document on Terminology of Non-proliferative Lesions developed by the GESC as an initial framework. It is understood that certain organ systems may need terms that are not covered in these documents. The OWG should produce a document that includes all appropriate nomenclature for its particular organ system.

- In general, the working groups should develop nomenclature that is primarily descriptive in nature and denote findings which can be documented from the review of routine histologic specimens. Incorporating specific diagnostic entities such as an infectious disease or that imply a process that cannot be ascertained from routine histologic specimens (e.g. phospholipidosis) is not recommended.

- For “systemic” lesions which may occur in more than one tissue (e.g. hemangiosarcoma), the OWG chair and GESC liaison should work with chair’s or other affected groups to determine most appropriate placement. In some cases, it may be warranted to have a general description of the lesion in one group (e.g. Cardiovascular group cover basic features of hemangiosarcoma) while other groups might provide additional details about the manifestation of the lesion in their manuscripts (Liver group cover features of hemangiosarcoma specific to liver.)

- An additional resource for the OWG’s are images from the National Toxicology Program (NTP). If the OWG does not have an NTP, member or liaison, contact your liaison for additional information.

**OWG Manuscript Review and Approval**

- Once the OWG has reached an initial consensus on the draft nomenclature, the GESC liaison will make the GESC aware that it is available for review.

- GESC review (30 days): The OWG will provide the GESC with the text of the draft nomenclature in word format. At this stage, GESC does not need to be provided the images for review. GESC members are expected to review for format, consistency, and content and provide their comments to the GESC liaison within 30 days.

- Revision and Upload to goRENI: The OWG will revise nomenclature as needed based on GESC review. Following these revision, the OWG will provide the updated text and images to goRENI (Rupert Kellner) for posting to goRENI.

- Member Review (60 days): Once the information is available on goRENI, a 60-day open comment period will begin. To encourage comments the following steps should occur:
Each society will notify their members via email and include both a link to goRENI as well as the document in word format.

- OWG Chair should consider actively soliciting input from key experts who may not be part of the OWG.
- GESC to send key leaders in pathology organization focused invitations to send comments from their organization

- Based on review comments the OWG will draft a “Print Publication” version of the nomenclature
- OWG submits final draft to GESC for final review and approval
- Following approval, the OWG chair and GESC liaison will facilitate publications and website finalization.

**Publication of Final Nomenclature**

- The final nomenclature documents will be available via:
  - Internet access as manuscripts on the goRENI site
  - Published from in toxicologic pathology journals
    - See appendix A for guidance on preparation of journal manuscripts

**Guidelines for Images**

Support is available for preparation of images; however, OWG should be aware of the following guidelines when acquiring images.

1. All images should be digital and of high quality (in focus, color-balanced, etc)
2. Images should be at least 6 inches wide @ 300 dpi
3. Images should be in a high-quality format: tif or eps (not jpg), using RGB color
4. Images should not be flattened
5. If an image has two parts (A&B), they can be combined on a single plate, as long as the other rules are followed
6. These guidelines will ensure quality images for print applications. Other applications (web-based, CD-ROMs, etc) can be prepared from images of this quality.

Each OWG should be aware that in addition to the existing images in goRENI, images may be available from the National Toxicology Program (NTP). If the OWG goes not have a member who has access to the NTP files, please contact your liaison to GESC for assistance. Images available in goRENI are available for publication, but will need to have copyright watermarks removed prior to publication. If images have been used in publication and are copyrighted, OWG will need to seek access or permission from the source journal.

When the OWG has selected images for their print publication, they are encouraged to contact Beth Mahler for assistance and consultation on preparation of images for print publication.
Appendix A

Guidance for Organ Working Group on Format of Nomenclature Documents for Journal Publication

Within the goRENI system, individual diagnostic entities are referred to as manuscripts as outlined in Appendix B. During the comment period, members of the respective societies will enter comments using the Forum feature. Following the web-based review period, the OWG will consider comments made in the forum section and make revisions as needed.

After revisions have been made to the individual diagnostic entities (manuscripts), the OWG will compile the terminology into an integrated publication that encompasses both proliferative and non-proliferative lesions. The content for an individual diagnosis (manuscript) is similar in both the web-based and the print format. The following are suggestions on organizing the print publication.

1. Title Page
   a. Title
   b. Authors and affiliations
2. General Introduction
   a. Brief overview of the organ system
   b. Purpose of the publication referencing the goals of the INHAND project
   c. If needed, comments on how the publication is organized
3. Nomenclature – OWG should determine how best to organize or group the individual diagnostic entities (manuscripts). For most organ systems this will be on an anatomic basis with respect to organ or tissue type. In general, non-proliferative lesions would be listed first, followed proliferative lesions. For most tissues, it may be useful to arrange the proliferative lesions in order from hyperplasia to benign neoplasm to malignant neoplasm for a given tissue type. As an example, for the basal epithelium of the skin, basal cell hyperplasia would be listed, followed by basal cell adenoma, followed by basal cell carcinoma.
   a. Introductory comments for organ/tissue (optional)
      i. OWG may desire to provide text to explain specific anatomic features, how the entities or organized, or other comments.
   b. Listing of Manuscripts (Diagnostic entities)
      i. Using the INHAND format shown in Appendix B
4. Figures: In general figures would be placed 6 per page and run at the end of the manuscript text. In some cases, the OWG working with the journal, may determine that placing pages of images after a specific organ, may be more useful. This decision should be made in consultation with GESC liaison, journal editorial staff, and OWG chair.
5. References should be cited within the text, but the reference list should be placed at the end of the publication.
Appendix B

Definition and Structure of a "Manuscript"

Within the INHAND nomenclature system, a manuscript describes the diagnostic criteria for one lesion, which may occur in one or more than one organ. Differences in diagnostic criteria among species (rat and mouse) should be mentioned in the text.

A manuscript consists of the following sections. Each of these sections can occur only once within a manuscript. Within a section, sub-headers may be used for e.g. species or modifiers, if diagnostic criteria differ among them. While the OWG shall determine the appropriate level of detail for each entity, the overall concept for the documents are concise descriptions of diagnostic entities that allow ready use by toxicologic pathologists. References are used to refer the reader to more in depth discussion of the entity.

Organ name(s) [mandatory]

At least one organ must be assigned here. More organs may be mentioned if a particular lesion occurs in more than one organ. If a lesion can be diagnosed practically in all organs, the location should be defined as

- Soft tissue
- Musculo-Skeletal system
- Peripheral nervous system
- Vascular system
- [Generally used preferred terms]

Names of organs should be given always in singular, also for paired organs. The lexicon contains the information whether an organ exists paired, but it is not mentioned in the name.

The organs listed here should include all organs, where one particular lesion can be found (e.g. amyloidosis is a systemic disease therefore the location should be defined as generally used preferred term). The lesion will then be listed under all these organs and can be easily reached via the organ or organ system selections in goRENI.

Lesion name [mandatory]

The preferred term for the lesion. If applicable, this is available in two variants with type of lesion first or descriptive component first. For example either carcinoma, hepatocellular or hepatocellular carcinoma

There are two configuration options in the web-based format goRENI, which allow individual users to see either one or the other variant. This affects alphabetical listing of terms and every occurrence of the names in the manuscript title and links to other manuscripts. For the printed publication the OWG should use the form in which the lesion is listed first eg carcinoma, hepatocellular.
**Biological behavior [mandatory]**

Is part of the lesion. The following possibilities are available:
- **M**: malignant tumor [systemic (malignant) tumors are included]
- **B**: benign tumor [polyps are included]
- **H**: pre-neoplastic lesion (usually hyperplasia or metaplasia)
- **N**: non-proliferative and non-proneoplastic proliferative lesion including reactive lymphoid hyperplasia

*Biological behavior of lesions is important in goRENI for the listing of lesions within one organ and appropriate icon selection. Lesions are listed according to these categories first and within one category in alphabetical order.*

**Sub-topographies [optional, non-proliferative lesions only]**

Possible sub-topographies for a diagnosis, like zona fasciculata, zona glomerulosa, zona reticularis in the adrenal gland.

**Synonyms [optional]**

Any list of names used (in the literature) synonymous for this lesion. As the preferred terms, synonyms should be available in two variants to be easily found in the goRENI index.

*Synonyms are used in goRENI to more easily find a certain lesion via the index. Sometimes, a lesion, although available, may be remembered by some pathologists under a different name. These could thus be directed to the right manuscript. All names used in the SSNDC guides and WHO/IARC fascicles should be included in this entity if not preferred term.

As the lesion names, all synonyms should be available in two variants with type of lesion first or descriptive component first.*

**Modifier [optional]**

List of modifiers, which can be used to sub-classify a lesion (e.g., according to a specific growth pattern or a distinct cell type). Criteria for using a modifier should be given in the section "Diagnostic Features" under sub-headings.

*The OWG should define if the use is obligatory or descriptive / facultative for a certain lesion.*

**Pathogenesis [mandatory]**

At a minimum, this section will describe the cell or tissue or origin for proliferative lesions. This section may also be used to describe key features of the pathogenesis or mechanism.
Microscopic Diagnostic Features [mandatory]

Bulleted list of essential diagnostic criteria to be used for a specific finding, including staining characteristics, size criteria or growth patterns.

For all neoplastic lesions it is recommended to give information on the following topics: localization, distribution, demarcation, compression, capsule, architecture, growth pattern, cells / nuclei, mitosis, size criteria, other (preferably in that order).

For non-neoplastic lesions localization, distribution, cells, other (preferably in that order).

Special Techniques for Diagnostics [optional]

If desired, additional diagnostic techniques that may be helpful in determining the diagnosis can be included. Emphasis should be placed on when these techniques are useful from entities in the differential diagnosis. Categories may include:

- Special stains, histochemistry
- Immunohistochemistry
- In Situ-Hybridization
- Electron microscopy
- Other special diagnostic methods

Differential Diagnoses [mandatory]

List of lesions with similarities to the currently described one. This list should be accompanied by the main criteria for differentiation that should be given in bulleted form (only differentiating diagnostic criteria need to be listed here). The list items should be connected by using OR or AND to advise users whether individual entries are indicative on their own or must occur in combination.

Comment [optional]

Any additional information regarding the description of the lesion which is not necessarily relevant for making a diagnosis.

This section should be structured by sub-headings, like

- Distinguishing macroscopic features
- Frequency of the lesion
  - Usual natural occurrence of this lesion in control animals (separated by sex), given as "extremely rare", "rare", "frequent". Remarks on the age-related occurrence should be included also.
- Pathogenesis
• Induced lesions
  Further comments on the induction of this lesion, e.g. by naming substance classes.
• Regulatory issues / remarks
  Any remarks regarding regulatory guidelines which need to be considered in certain studies when diagnosing this lesion.

References
Literature should not be older than 15 years, except fundamental and important papers. The citation format should be identical to the existing manuscripts / lesion descriptions. If abstracts in PubMed are available, links will be included.

The citation format should be identical to the existing manuscripts / lesion descriptions, as a transformation to the format for the different journals (ToxPath, Exp Toxic Pathol, Jap J Path) can be easily done by a computer program. The references should be given for each individual manuscript / lesion. For printing in the journal, redundant information for a whole organ system can be removed and references placed at the end of the manuscript. For goRENI it is useful to have the references lesion specific.

Images
Categories:
  o Gross lesions (naturally occurring lesions / induced lesions)
  o Micro photographs (naturally occurring lesions / induced lesions)

Preferable data in the legend:
  o Organ, lesion, modifier
  o Spontaneous vs. induced (by ...[type of compound])
  o Strain (breeder), sex, age, animal status
  o Further description ...

Please fill out at least the following template:
  • Rat / Mouse
  • Organ
  • Lesion
  • Modifiers [if applicable]
  • Stain [e.g. H&E]
  • Magnification [e.g. x20, object lens only]

The following information should be supplied if available:
  o Sex: male / female
  o Age: ... days
- **Strain**: ...
- **Animal status**: scheduled death / killed moribund / died

**For goRENI the number of images is not restricted. For the printed publication the OWG should select a limited number of images for each entity.**

**Trimming**

Links to the trimming guides (if applicable) will be automatically inserted by the software (see [http://reni.item.fraunhofer.de/reni/trimming](http://reni.item.fraunhofer.de/reni/trimming)).

*The links are supplied in goRENI to conveniently reach the trimming information. This will not be used in the printed publication, but can be referred to in introductory comments.*