

*Tissue accountability* is an important factor to judge the quality and validity of toxicity and in particular of life-time bioassays (48,86). It is influenced by various factors, such as autolysis, age of the animal (e.g., thymus), size of organ, amount of tissue available and preserved during necropsy, and embedded in paraffin blocks. There are no guidelines, but a recommended minimum standard for life-time bioassay studies is 90%/sex/group with the following exceptions or specifications (75):

- Parathyroid glands: for at least 70%/sex/group sufficient tissue from at least one gland
- Adrenal glands—cortical and medullary tissue available bilaterally in at least 70%/sex/group and unilaterally in 90%/sex/group
- Thymus: for at least 80%/sex/group
- Mammary gland—rat  
Males: for at least 90%/group a section of subcutaneous tissue from the mammary area (caudal portion of the ventral abdomen) with or without male mammary gland  
Females: for at least 90%/group subcutaneous tissue with mammary gland components
- Mammary gland—mouse: similar to rat, but for both males and females at least 70%/group

*Blinded slide evaluation* means evaluation of slides without knowing the treatment group. It is not recommended for routine examinations (87). However, blinded reading of an organ with an equivocal or subtle finding can be very helpful. If done, it should be recorded in the raw data and the study report and this will enhance the confidence of the regulatory reviewer on the validity of the data (75).

In addition, *peer reviewing* has become a standard procedure in pathology (88–90). Specifically, a pathology colleague examines a selection of the histological slides of a study. This can mean that 10% of all animals at random plus all target organs are re-examined by the reviewing pathologist. The procedure has to be recorded; in particular discrepancies and their resolution should be noted.

### 3. GENERAL PATHOLOGY

An organism and its organs/tissues have a limited spectrum of reactions to non-physiological conditions, including toxicity and carcinogenicity.

This section defines the basic pattern of reactions, provides some insight into the pathogenesis of these basic lesions, and addresses their consequences as far as relevant for toxicology.