



Single or Repeat-Dose Toxicity

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This protocol assumes an intermediate level of scientific competency with regard to techniques, instrumentation, and safety procedures. Rudimentary assay details have been omitted for the sake of brevity.

*Some of the NCL's experiments are tailored specifically to the individual nanoparticle under study. As such, a standard experimental method cannot be generated. Instead of a protocol, we offer the following brief description of the experiment and the types of data it generates, to aid in determining a suitable experimental pathway for a nanoparticle characterization project. The following description is **not** a protocol and does not describe all of the relevant experimental parameters necessary to conduct the experiment. If you'd like more information, please feel free to contact us at the phone number or email address provided on the previous page.*

Single or Repeat Dose Toxicity

Each NCL *in vivo* study is tailored to the particular compound being tested, so each toxicity study is a little bit different, but "normally", we conduct single or repeat-dose toxicity tests, usually in both male and female rats or mice, usually i.v. administration via tail vein injection. We monitor the animals usually for up to 14-days, though sometimes longer if we expect longer term toxicities (28 days for immunotoxicity). We look for any changes in mortality, body weight, organ weight, clinical chemistry, hematology, gross pathology, and histology of both control and treatment groups, usually in comparison to free/active drug and to clinically available alternatives. We look at many different tissues (brain, heart, kidney, liver, spleen, lung, etc.), and look for lesions and statistically significant differences in organ weight between treatment and control groups. The doses used in this study depend on the expected clinical dose, the available material, and in the volume of material we can inject. Ideally, we test the expected clinical dose (scaled by body weight or surface area to rats) and 10 and 100-fold times that dose.

All NCL studies are conducted under non-GLP conditions, but ICH guidance indicates that non-GLP acute toxicity studies can be sufficient for an IND as long as repeat dose acute toxicity studies are conducted under GLP conditions.

Tissues Evaluated by Histopathology

- brain
- pancreas
- salivary gland
- lymph node
- esophagus
- parathyroid
- thyroid
- trachea
- adrenal
- pituitary
- heart
- kidney
- thymus
- gall bladder
- liver
- spleen
- lung
- duodenum
- ileum
- rectum
- stomach
- cecum
- colon
- jejunum
- epididymis
- ovary
- prostate
- seminal vesicle
- testis
- urinary bladder
- uterus
- eye
- Harderian gland
- nasal sections
- femur
- femoral artery
- vertebra
- spinal cord
- mammary gland
- skin/subcutis
- tongue
- and any additional tissue with gross findings at necropsy

Hematology Parameters Evaluated

- erythrocyte count (RBC)
- hemoglobin (HGB)
- hematocrit (HCT)
- mean corpuscular volume (MCV)
- mean corpuscular hemoglobin (MCH)
- mean corpuscular hemoglobin concentration (MCHC)
- platelet count (PLT)
- reticulocyte count (RETIC)
- total leukocyte count (WBC)
- differential leukocyte count
- nucleated red blood cell count
- blood smear

Clinical Chemistry Parameters Evaluated

- blood urea nitrogen (BUN)
- aspartate aminotransferase (AST)
- alanine aminotransferase (ALT)
- gamma glutamyl transpeptidase (GGT)
- glucose (GLUC)
- creatinine
- total protein
- albumin
- globulin
- albumin/globulin ratio (A/G)
- sodium
- potassium
- chloride