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Pre-clinical toxicology considerations in vaccine

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Careful considerations in any pre-clinical toxicology vaccine study will help in collecting vital, precise, information which will help in designing the proper clinical study. Infiltration of inflammatory cells at the site of injection, decreased food consumption, loss of body weight or elevation in body temperature findings in the pre-clinical toxicology study are the counterparts for inflammation and pain at the site of injection, malaise, fatigue and slight febrile responses produced by vaccines in the clinical study. Thus, proper design and techniques (e.g., sampling sites, type of anesthesia etc.) used in any pre-clinical toxicology study for vaccines is very important. Multiple factors should be taken into consideration when analyzing the final outcome of any toxicology study. Careful considerations should be given to site of blood collection, food intake, stress, and age-related changes. Sampling sites (tail, foot, eye and heart) affects the values for murine white blood cell counts and other hematological parameters. Moderate to severe food restriction causes decreases in reticulocyte, neutrophil, lymphocyte and platelet levels in rats. Acute restrain stress decreases monocyte and lymphocyte levels and increases neutrophil levels in rats. Anesthesia is another example of factors that may alter the outcome of toxicology studies. Choosing the type of anesthesia (CO2, isoflurane, pentobarbital, and ketamine/xylazine) is an important factor influencing the results of clinical pathology. When compared to CO2, isoflurane, pentobarbital and ketamine/xylazine caused increase in aspartate aminotransferase (AST) levels and decrease in total protein, albumin and triglyceride levels. Blood volumes that are drawn on a weekly or monthly basis from each animal should not affect the clinical pathology results. For example, on a weekly basis, blood collected from mouse, rat, dogs, monkeys and rabbits not to exceed 0.075, 1, 50, 10 and 10 mL respectively. Increases in blood volume collection above this specified volume for each animal species may significantly alter hematology and or clinical chemistry parameters levels. Acute phase reactants [APR] (e.g., C-reactive protein, Haptoglobin, fibrinogen, serum amyloid, albumin, pro-inflammatory cytokines, alpha1-acid glycoprotein (α1AFP), α2-macroglobulin (α-2M) and thiostatin) are used in the assessment of inflammation. The suitability of each APR as a marker of inflammation depends upon certain criteria. Additionally, validating sample collection time points for specific protein should be carefully considered. Other factors like the quality assurance elements (SOPs, instrument validation, lab certification etc.) should also be considered.

Biography

Nabil Al-Humadi is currently working as a Pharmacologist at the Center of Biologics in the US Food and Drug Administration. He holds two Master degrees and a PhD degree and he has 18 years' of work experience in the government and 7 years in the industry. He has currently published a chapter entitled "Pre-clinical toxicology of vaccines" in "*Comprehensive guide to toxicology in preclinical drug development*" book.

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