

AUBURN UNIVERSITY

Institutional Animal Care and Use Committee (IACUC)

Policy on the Use of Adjuvants

There are a number of adjuvants of interest to the IACUC. Of principal interest is the nature of the adjuvant, especially if it is Freund's Complete Adjuvant (FCA) injected with the antigen to augment the antibody response. FCA commonly causes adverse side effects. Negative effects routinely seen include granuloma formation, tissue necrosis and sloughing, abscessation, and fever. Other deleterious systemic effects, such as polyarthritis, have been reported. FCA is considered a human biohazard, such that accidental self-inoculation or splashing in the eye has been shown to cause painful sequelae not readily amenable to treatment, as well as sensitization to tuberculin. Adverse reactions to FCA vary according to the anatomical site in which it is placed, the volume of antigen used, and the purity of the antigen. Due to the occurrence of adverse reactions, discontinuance of the use of FCA has been advocated in favor of alternative adjuvants such as Ribivax and TiterMax.

Policy:

Less inflammatory alternatives to Freund's adjuvant are available and should be considered. Ribivax Adjuvant System® and TiterMax® are commonly cited as appropriate alternatives. Non-inflammatory adsorptive adjuvants such as alum and aluminum hydroxide gel should also be considered. The use of FCA as an adjuvant is permitted if the investigator provides scientific justification for its use, rather than less irritating adjuvants.

In regard to the use of FCA in rabbits for polyclonal antibody production, the following guidelines apply:

If FCA is to be used, it should only be used for the first (priming) antigenic dose. Using two or more doses of FCA is rarely warranted. Subsequent doses with antigen should utilize Freund's Incomplete Adjuvant (FIA) or another appropriate adjuvant.

The recommended injection protocol for FCA and FIA in rabbit immunizations are:*

- IM 0.5 cc (in two 0.25 aliquots)
- SQ 1.0 cc (in four 0.25 aliquots)
- ID 0.5 cc (in five 0.1 aliquots)

*Please note that the alternative adjuvants such as the Ribivax Adjuvant System® provide specific guidance regarding injection sites and volumes in the various species.

A total volume of 1.5 cc of the FCA or FIA/antigen mixture could be injected in a single immunization by injecting 1.0 cc SQ and 0.5 cc either IM or ID (intradermal). Injecting excessive volume in one site can cause major problems so it is important to follow the dosing aliquots given above. On the IACUC animal subjects review form (ASRF) the route of administration, the volume injected per site, and the number of sites injected must be described.

Footpad or intravenous injections of FCA are not allowed.

With the injection of any material, the inoculum must be free of extraneous microbial contamination. Millipore filtration of the antigen before mixing with adjuvant is recommended when possible.

Injection sites should be cleaned and free from debris and contamination.

The frequency of boosters must be described in the animal use protocol. Two to three weeks is generally considered the minimum time period between the initial and subsequent immunizations. Booster immunizations are sometimes delayed if significant inflammatory reactions are still present from the initial immunization.

REVISED: December 18, 2012