

University of Massachusetts Medical School
Registration Number 14-R-0035
Addendum to Annual Report of Research Facility (Form 7023c)
Fiscal year 2019

Explanation of Category E Studies:

Category E *in vivo* testing was performed under Dockets A-2184 and A-2207, of the Massachusetts Biologic Laboratories (MBL), located at the University of Massachusetts Medical School University Campus using death as an endpoint assays mandated by the Code of Federal Regulations. The assays are mandatory and required in order for MBL to maintain licensure to manufacture and distribute vaccine products.

A-2184 (190 Guinea pigs)

21 CFR 610.1 and 21 CFR 610.10 (requirement for potency testing of each lot of FDA licensed biological product)

21 CFR 211.166 (requirement for a stability testing program for FDA licensed drug products)

Diphtheria potency testing uses death as an endpoint. The current assay does not allow for the use of analgesics without FDA approval. Any pain-relieving drugs used to alleviate pain or distress may alter the disease progression in the established model and may interfere with interpretation of the results.

A-2207 (65 Guinea pigs)

21 CFR 211.84 (Requires the testing of each lot of drug components to be used in manufacture. The Public Health Service, National Institutes of Health, dated March 1, 1947 (tetanus) and revision December 15, 1952 (diphtheria) stipulate that the potency of the parent toxin must be evaluated either by *in vivo* titration against standard antitoxin or by the MLD method. Both methods involve toxin induced symptoms and death of guinea pigs as an endpoint. The MLD method can be accomplished using fewer animals and thus is selected for use.

Tetanus and diphtheria MLD assay: death by intoxication is the required assay endpoint. The current assay does not allow for the use of analgesics without FDA approval. Any pain-relieving drugs used to alleviate pain or distress may alter the disease progression in the established model and may interfere with interpretation of the results.

04 NOV 2020