(1) Hematological toxicity study; (2) Teratology study; (3) Thirty day IV toxicity study; (4) Metabolism study; (5) Mutagenicity study; and (6) Chronic and carcinogenicity study, including limited reproduction studies.

The research would be split between FDA in-house work and studies conducted under contract. The No. 6 priority oral chronic and carcinogenicity study was estimated to run for three years at a cost of $300,000, and it would be conducted under contract.

The FDA Committee said the "only documented injuries resulting from ETO have been of an acute nature and resulted from adulteration of medical devices and a medicated gauze pad with excess residues of ETO because of improper sterilization procedures." The group said, "There is no evidence of any injury to man/animal from chronic contact with articles manufactured under good manufacturing practice."

The report said, "When properly used and controlled there is no known hazard to the health of man/animals from the use of ethylene oxide for sterilization/fumigation."

ETO has been cleared under a Food Additive Order (§121.1232) for fumigation of spices and other seasoning materials, except mixtures to which salt has been added, with residues limited to 50 p.p.m. It also has been cleared as a fumigant in sizing for paper and paperboard in contact with dry food, as a modifier of industrial starch under §121.2506 for industrial starch-modified, and as a reactant with fatty triglycerides and their derivatives under §121.2519 for defoaming agents used in the manufacture of paper and paperboard.

Intramammary products may be sterilized by ETO if they are approved under New Animal Drug Applications. The Committee said that "such products have been and will be evaluated on a product-by-product basis," noting that any ETO residues in food would require a Food Additive Order.

The FDA group noted that the Environmental Protection Agency regulates pesticide use of ETO (See FOOD CHEMICAL NEWS, Feb. 25, 1974, Page 2), and has registered its use on black walnuts, copra, and whole spices, with residues limited to 50 p.p.m.

The residues involved when ETO is used are ETO, 2-chloroethanol, and ethylene glycol.

MANTEL-BRYAN PROCEDURE IRRELEVANT TO PCB'S: FDA

The Food and Drug Administration has declared that the Mantel-Bryan statistical procedure for determining the needed sensitivity of method for carcinogens is irrelevant to polychlorinated biphenyls and to other "poisonous and deleterious substances" regulated under §406 of FDA's law.

The American Paper Institute had hit FDA's failure to submit material dealing with Mantel-Bryan procedures in the record of the PCBs-in-paper hearing or in response to API's Freedom of Information request (See FOOD CHEMICAL NEWS, Sept. 29, Page 6)

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FDA Assistant Chief Counsel for Enforcement Alan Bennett declined to furnish the information in a letter to Stephen M. Truitt, of the Washington law firm of Wald, Harkrader and Ross. In addition to saying that Mantel-Bryan is not germane to the PCB proceeding, the FDA-er also said his agency fulfilled the FOI request, commenting that "the quoted portion of your request was, in our view, directed to data pertaining to the toxic and carcinogenic effects of PCBs, especially those effects stemming from low-level exposure over long periods of time."

Although FDA denied the relevance of the Mantel-Bryan procedure to the PCB matter, Bennett indicated that the agency is wedded to the procedure in the case of feed additives. A proposal on sensitivity of method for animal feed additives was based on the Mantel-Bryan method, and a draft revision of the proposal still being massaged within FDA is based on a modification of that procedure. Indicating Bureau of Foods adherence to the proposal for feed additives, Bennett wrote:

> "It is the Bureau's position that the M-B procedure is a valid concept in establishing the required sensitivity of assay methods where a particular additive or drug is intentionally added to animal feed or administered directly to an animal to obtain some advantageous result. In such a situation, FDA is able to regulate the length of time the additive or drug is used in the animal, set permissible dosage levels, specify methods of administration, and establish a withdrawal period before slaughter."

"Emphatically" rejecting Truitt's "contention" that the material should have been submitted in the PCB matter, Bennett said the Mantel-Bryan procedure "has absolutely no applicability to a proceeding designed to set a tolerance for a ubiquitous environmental contaminant such as PCBs."

He said the procedure "has been proposed as one statistical model that may be used in determining whether a practicable method exists to determine the absence in food of residues of potential or actual carcinogens intentionally fed to animals ...," but that it "was never intended to be, and would be inappropriate as, a mechanism to establish so-called 'safe' levels for environmental carcinogens in the human diet." Environmental contaminants, he added, "have no function in food." Bennett continued:

> "Assuming arguendo, that the M-B procedure were used to establish 'safe' levels for dietary intake of PCBs in humans, FDA must have the discretion necessary to determine how best to meet that level, consistent with the public health. Since exposure of foods to PCBs by packaging the food in contaminated recycled paperboard is easily eliminated through industry monitoring of the paperboard supply ..., through the use of impermeable barriers, or through the use of virgin paperboard, it is eminently reasonable, from a public health standpoint to minimize exposure from this source, particularly since it does not involve banning a significant portion of the nation's food supply."

§406 of the law, unlike §409, §512, and §706, "does not require that the Secretary establish an assay method adequate to determine that no residue remains in animal tissue," Bennett wrote, saying that §406 "has its own distinct criteria for setting a tolerance." He said FDA is required under §406 "to take into account the extent to which PCBs cannot be avoided and other ways in which the consumer may be affected by the same or other poisonous or deleterious substances."

If the Mantel-Bryan procedure were applied to environmental contaminants, there would be "unfortunate results inconsistent with protection of the public health," the letter said. Bennett explained:

> "In many instances, the M-B 'safe' figure would be so far below the level it is possible to attain that large portions of our food supply would have to be banned, despite the fact that the presence of very small quantities of environmental contaminants may present no health hazard whatsoever. In other circumstances, the M-B procedure may not adequately take into account the avoidability of a particular contaminant or the ways in which the consumer may be affected by similar poisonous or deleterious substances, and the level may be set too high."

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FDA ASSERTIONS IN PLASTIC BOTTLE EIS QUESTIONED BY EPA

Food and Drug Administration assertions contained in the agency's draft Environmental Impact Statement (EIS) on plastic bottles (See FOOD CHEMICAL NEWS, Aug. 11, Page 19) have been questioned by the Environmental Protection Agency's Sheldon Meyers, in a letter to Charles Custard, Director of the Environmental Affairs Office in FDA's parent Department of Health, Education and Welfare.

Noting questions he had raised earlier concerning FDA's EIS (See FOOD CHEMICAL NEWS, April 28, Page 28), the Director of EPA's Office of Federal Activities expressed concern about FDA's assessment of possible dangers from emissions of toxic gases and questioned the agency's acceptance of "the statement, attributed to the National Center for Resource Recovery, Inc. ..., that 'plastics do not create a problem in sanitary landfills because they do not deteriorate or contribute to contamination of ground or surface water and are equivalent to inert materials such as glass, concrete, and aluminum, helping to stabilize the fill.'"

Meyers said that EPA's concern about the toxic gases released by combustion of acrylonitrile containers "is based on more than 'speculation' as implied in the EIS," explaining that where combustion is not complete, combustion products "are known to contain harmful quantities of hydrogen cyanide, acrolein, and other toxic gases."

If such gaseous emissions are drawn into apartments through open windows or a ventilation system, following incomplete burning of the bottles in an apartment-type incinerator, Meyers pointed out, "the health of the residents might be seriously jeopardized."

MONS 032515