Dr. LEGATOR. Fine.

Mr. DUFFY. Mr. Chairman, before Dr. Legator begins, I have been asked to make it clear for the record that although Dr. Legator is an employee of the Food and Drug Administration, he appears here today in his own behalf; the opinions he expresses in no way represent the official opinions of his employer. Is that correct, Doctor?

STATEMENT OF DR. MARVIN S. LEGATOR, CHIEF, CELL BIOLOGY BRANCH, DIVISION OF PHARMACOLOGY, BUREAU OF SCIENCE, FOOD AND DRUG ADMINISTRATION

Dr. LEGATOR. Thank you for making that statement.

Mr. DUFFY. Is that correct, Doctor?

Dr. LEGATOR. That is correct. And I do understand that the Commissioner of Food and Drugs will appear later on in the committee hearings to answer any matters pertaining to policy.

If possible, I would like to read my statement through, and defer any questions until the end of my presentation.[1]

The end of the 1960's witnessed the discovery that a succession of chemicals including food additives, pesticides and drugs were found to be chronically toxic to animals. The agricultural fungicide Captan was found to be mutagenic and produce congenital malformations; DDT was reported to be carcinogenic in mice; cyclamate produce chromosome abnormalities in rats; bladder tumors when orally fed to rats and congenital malformations when injected in the chick embryo; and the antifungal antibiotic, griseofulvin produced hepatomas in mice and one could quote many other examples.

In each of the cited examples we are dealing with substances that have been on the market for several years and in some instances decades. The toxic response in each instance is in the area of chronic toxicity and more specifically that area that I will refer to as genetic toxicity. I would like to define genetic toxicity as three types of responses that may lead either to a carcinogenic teratogenic, or mutagenic effect. Table 1 indicates the probable mechanism and differences betwen these three types of genetic responses.

Never have so many healthy individuals of child-bearing age been exposed for a prolonged period to a drug for nontherapeutic use. The uniqueness of the hormonal contraceptives make it important that a careful evaluation of potential hazards in the area of genetic toxicity be carried out. In 1965, one of every four married women under the age of 45 had used or was using oral contraceptives. Actual users in 1965 numbered 3.8 million and an additional 2.6 million had discontinued use. Almost three out of four American women starting oral contraceptives continued to use the method for at least 1 year and more than three out of five continued for at least 2 years. Estimates of the number of current users indicate an apparent doubling since 1965.

What types of studies are required to give us greater assurance of minimal genetic effects? To answer this question, I will discuss certain general principles that apply to substances that are either mutagenic,

[1] The complete prepared statement and supplemental information submitted by Dr. Legator begins at p. 5952.