which the Food and Drug Administration had ruled to be subject to the restrictions under the Drug Abuse Control Act.

The most dangerous drugs have been withdrawn from the market or not permitted to be marketed in the first place. Other drugs, addictive derivatives of opium, have been placed under the strict controls of the Narcotics Bureau. But there is an important third category of drugs, including the barbiturates and amphetamines, which are of proven value and far less dangerous, which have been found only recently to be subject to abuse and have hence been made subject to the Drug Abuse Control Act.

The removal of a product from non-prescription status, or if already a legend drug the placing of that product under the restrictions of the Drug Abuse Control Act, is likely to have a depressing effect on sales and as such must be considered as one of the risks facing the industry. It is difficult and often impossible to quantify the loss in such cases. Smith, Kline & French has estimated the loss of sales on its amphetamine products due to the new Drug Abuse Control Act restrictions at about 20 percent for this important category of its product line.

(*d*) *Risk Factor No. 4.*—Risk of withdrawal or restriction of products pending additional evidence of safety and efficacy (p. 2821).

It is difficult in many cases to determine whether a given example falls under this heading or under the category of risk from unforeseen side effects. The example cited by Professor Markham—MER 29—was a case in which a drug was withdrawn on the basis of unexpected side effects. The example of Imferon, mentioned above, is another case in point.

It is too early to determine the full effects of the current efficacy review of pre-1962 drug products. The most important category of products so far affected is that of the bioflavinoids. For some companies, especially smaller ones specializing in vitamins, this decision by the FDA has had a serious financial impact.

(*e*) *Risk Factor No. 5.*—Risk arising from a problem of quality control (pp. 2823-24).

Quality pharmaceutical houses maintain extensive and elaborate control laboratories and procedures. Such firms strive for perfection constantly, within reasonable economic cost limits, but absolute "zero-defects" has never proved possible in any system yet, despite highly sophisticated control mechanisms coupled with human judgment. With billions of tablets produced annually both machine and human error may occur—and when it does, it may be exceedingly costly. Because of the nature of the product, the effect of such error can be far more serious, both for the consumer and for the manufacturer, than in other types of manufacturing. An error in labeling, for instance, may cause considerable danger or it may be relatively innocuous, but the recall of products resulting from such mistakes usually is very costly.

An example of this type of risk is the Cutter vaccine incident cited by Professor Markham. See Point 7 above.

Under this same heading of risk arising from quality control problems, mention should be made of the danger of the contamination of one product by remote traces of another. This situation, leading to the recall of products from the market, can arise, of course, from the fallible human element, despite all the safeguards established under the high standards which the pharmaceutical companies set for themselves. But it can also occur as a result of changes, sometimes unexpected, in Government standards or regulations, so that products which formerly fell well within the prescribed tolerance limits are suddenly subject to recall, with little or no advanced notice and with all the loss, both financially and in prestige, which such recalls entail.

Industry witnesses have already testified about the unforeseen investments required as a result of more stringent regulations being imposed to eliminate even a trace of penicillin contamination of other products. In at least one case this compelled a major company to build an entirely new factory some miles distant from its other plants. Many have had to incur substantial costs of pulling products back from wholesalers and retailers. The quality control problem may even be due to error on the part of the authorities. The February 12, 1968 issue of the F-D-C Reports (Pink Sheet) cited the example of an FDA recall of 27 million tablets of a heart drug which appears to have been due to a technical error in the assaying techniques used by the FDA's inspection authorities. The USP, whose assay directions were used in this case, announced that discovery of an "un-