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DES. It appears, in fact, that if Ralgro is substituted for DES, the same fat saving (if any) would result. If bulls were raised as an alternative to treated steers, fat content would apparently be decreased. It is, in any case, not clear whether the indicators of fat content in these studies are significant in the real world. For example, if the fat on a steak is of the type that would normally be trimmed by the butcher, or by the cook or consumer prior to eating, then that fat would not have any adverse effect on the consumer. (Presumably, where the reports speak in terms of marbling, the fat in question would not normally be trimmed before consumption.)

(b) Amount of Beef and Lamb That Will Be Consumed. Another factor in the computation of the potential increase in fat in the human diet from the withdrawal of approval of the DES NADA's is, of course, the amount of beef and lamb that a human being would reasonably be expected to consume. Nothing in the record tells us how much lamb a person may be expected to consume. The CAST Report (M–51 at 26) cites a 1976 Department of Agriculture economic research service report as calculating the average consumption by Americans of beef as 2.3 pounds of "carcass weight equivalent" per person per week. Apparently, the actual amount of beef consumed would be smaller since the "carcass weight equivalent" would include the nonedible portions of the animal's carcass.

Estimates of the amount consumed were also given by manufacturing parties' witnesses seeking to compute a total risk to humans from the use of DES. See, e.g., M–63 at 261–62. They estimated the average intake of beef per day variously at 140 g and 284 g for purposes of calculation. If, as the manufacturing parties seem to argue, the withdrawal of approval of the NADA's for DES would decrease the availability of beef to the public, then the amount of beef consumed would decrease. If, as predicted by the manufacturing parties, beef prices increase when DES is no longer available, that price increase might lead to a decrease in beef consumption (M–51 at 26). A decrease in beef consumption would, of course, tend to carry with it a decrease in the consumption of beef fat. The magnitude of this decrease in overall beef consumption and its impact on total consumption of fat cannot be determined from the record. Nor does the record show how this decrease in fat would compare to the increase that the manufacturing parties project would result from discontinuance of the use of DES.

(c) Amount of Fat in Alternatives to Beef and Lamb. The record contains little information about the potential substitutions likely to be made in the diets of Americans if, in fact, the amount of beef available is decreased, or consumption is lowered due to price increases, as a result of the withdrawal of the approval of the DES NADA's. That substitutions would occur is emphasized by an intervenor's exhibit (PA–22), which is an attempt to predict the economic impact of restricting feed additives in livestock.

In a simulation dealing with the ban of DES, the authors of PA–22 calculated price effects not only in beef, but also in pork, broilers, and turkey. (The amount of lamb produced in this country is apparently so small, relative to the amounts of other meats, that it was not considered in this analysis.) The effect on the prices of these other meats caused by a decrease in availability of or rise in the price of beef assumes that the American consumer will substitute these other meat products for beef if use of DES is no longer permitted. Thus, it is important to know what the fat content of these alternative meats is. This information is not in the record. The failure to take into account the amount of fat involved in the eating of alternative meat (or other) products would presumably result in a faulty computation of the effect of a ban of DES on fat in the diet.

It is noteworthy that one manufacturing parties' exhibit states that a ban of DES, if it decreases the amount of beef consumed, will lead to consumption, in the alternative, of cereal products (M–51 at 26). Presumably, this change would result in less total fat intake in the average diet.

(iii) *Conclusion as to Claimed Health Benefit From Decreased Consumption of Fat.* The Administrative Law Judge found, in essence, that the manufacturing parties had failed in their burden of showing benefits of DES. An analysis of the claim that DES has a health benefit in reduction of fat shows that the Administrative Law Judge's conclusion with respect to that claim was correct. The record simply fails to support the contention that DES provides a health benefit by reducing dietary intake of fat.

(d) *Health Benefit: Feed Saving.* The manufacturing parties cite as a second health benefit of DES the saving of food that results from the feed efficiency associated with the drug (Manufacturing Parties' Exceptions at 177). The manufacturing parties rely on the testimony of Dr. Jukes that the feed-saving value of DES is estimated (he did not say by whom) at 7.7 billion pounds annually and as being equivalent to 3 million to 4 million acres of corn (M–99 at 17–18). Dr. Jukes then stated that a yield of 150 to 175 bushels of corn per acre per year would supply an additional ration of 500 calories per day per person to 80 percent of the world's hungry people (id.). (Dr. Jukes apparently assumed that the saving in animal feed grain would result in the production of more human food grains.)

Dr. Jukes' argument is curious, since presumably the amount of feed that DES saves is presently available. Thus, if this food is not being used at this point to supply the additional calories to 80 percent of the world's hungry people, there is not much to be said for the argument that DES use should be continued so that this excess food capacity will be available.

The Administrative Law Judge noted that any prospective grain saving from DES would be of less importance because there is presently no grain shortage in the United States, where the grain savings would, of course, be generated. As the manufacturing parties argued, the question properly is whether, if DES were no longer available, there would be a grain shortage. In fact, the testimony cited by Judge Davidson supports the proposition that, at the time of cross-examination, there was a surplus of grains (Tr. at 2014). Because the record does not reveal whether any increase in grain consumption associated with the unavailability of DES would be greater than any present surplus of grain, it has not been shown that a ban of DES, even if it did increase grain consumption, would lead to shortage.

Evidence in the record suggests that the unavailability of DES might not have a very significant effect on the fluctuating grain situation. A Department of Agriculture Economic Research Service report (PA–28) that is undated but utilizes 1969 figures notes that cattle finishing (the stage at which DES is most often used) accounts for only 16 percent of all feed grain use (id. at vi). (Thus, even if the unavailability of DES increased grain consumption in feed lots to some extent, the effect on the total grain supply would not necessarily be great.)

This report's projection of the different possible effects of a DES ban illustrates the difficulty involved in making this type of estimate. The report, which assumes the absence of alternative growth promotants, considers the effects of three possible results of the ban: (1) feeding the same number of cattle for the same length of time (and thus producing less meat per animal); (2) feeding the same number of

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cattle for longer periods; and (3) feeding a larger number of cattle for the same period (id. at v). The report acknowledges that the actual result would probably be some combination of these options (id.). (Since this report was apparently prepared without the benefit of data from the ban of DES in the early 1970's, its projections are necessarily more speculative than those discussed below in the economic benefits section.)

The report projects that option (1) would result in a reduction in feed consumption of 2 percent (id. at vi) (feed consumption would be reduced because untreated cattle consume less feed per day than DES-treated cattle); option (2) would result in a significant increase in feed consumption (no percentage is given) (id. at vii); option (3) would result in a 2.1 percent increase in feed consumption (id.). The report then states that option (2) (in which the ban of DES results in an increase in feed consumption over consumption associated with DES treatment of cattle) would result in a $100 million saving to the economy because the increase in feed consumption would reduce the costs of the feed grain program! (Id.)

A manufacturing parties' document—Council for Agricultural Science and Technology, *Hormonally Active Substances in Foods: A Safety Evaluation*, Report No. 66 (March, 1977) (CAST Report) (M-51 at 26)—notes that the ban of DES, assuming it results in a decrease in efficiency of feed utilization in beef production, would be expected to have little effect on the release of grain for world trade. The report notes that, as feed efficiency increases, the price of beef decreases which, in turn, encourages more consumption of beef and, thus, more production, followed by the use of more feed to produce that beef. When efficiency decreases (as it would in the absence of DES and other growth promotants), the price of beef rises, consumption decreases, production of beef decreases and more grain is available. On the other hand, presumably any consumption decrease will be associated with a turn by consumers to other meats and to cereal grains. This increased consumption of cereal grains might itself have some effect on food grain availability. The CAST Report does not discuss this possibility, however.

The manufacturing parties do not present evidence on the loss of grain, and on the effects of that loss, during the 1974 ban of DES. Perhaps more important, moreover, the manufacturing parties do not present evidence of the amount of grain loss that could be expected if, as would be logical, beef producers turn to other growth promotants when DES is no longer available.

It is simply not possible from the evidence in this record to determine whether and to what extent the withdrawal of approval of the DES NADA's will affect the availability of feed grains. Even if there were a decrease in the availability of feed grains, it is not possible to determine whether and to what extent that decrease would result in a decrease in food that would otherwise be made available to, and would provide a health benefit to, human beings.

(e) *Economic Benefits.* The nonparty participants state their position that DES produces an economic benefit boldly: "If DES really has no value, then as a practical matter *it simply won't be used*" (emphasis in original) (Intervenors' Exceptions at 5). This argument has a strong initial appeal. DES, without question, enjoys wide use, presumably by people who believe it is in their economic self-interest to use the drug. Yet the FDA's experience with human drugs counsels skepticism toward a claim that something is true because most people believe it to be true. (Many such drugs have been widely used for years, only to be found later, upon objective test, to be worthless.)

The record in this proceeding contains little support for the proposition that DES provides a significant economic benefit to society that would not be provided by available alternative growth promotants. More important, the record provides no reliable basis for determining how great the economic benefit of DES, if any, is. Nor does the record make possible a decision as to who receives any economic benefit associated with the use of DES as an animal drug.

As I have discussed in section III(E)(1), I am not authorized by statute to decide that an animal drug is "safe" because the economic value of that drug is more important to society than the risk of cancer it poses to consumers. If I were so authorized, I could not make a responsible decision without substantial evidence that DES does provide an economic benefit, and without substantial evidence showing how great that benefit is and to whom it accrues.

The proponents of DES use have done a very poor job of providing information to this record on this issue. No expert economist testified, though the task of forecasting the economic effects of the unavailability of DES is complex. Despite the fact that DES been removed from the market previously (premixes for more than a year, implants for 9 months), the proponents of DES use have presented no careful analysis of the economic results of that action. As discussed above, the manufacturing parties have the burden of proof on the risk/benefit issue, if that issue is appropriately a part of this proceeding at all.

(i) *Does DES Provide an Economic Benefit?* Without question, DES provides an economic benefit to the drug companies that make and sell it. Presumably even if I were required to make a risk/benefit analysis of DES, I could safely disregard that benefit. The discussion that follows thus considers the evidence in the record that use of DES as an animal drug provides economic benefits to other segments of society.

To determine correctly whether the withdrawal of approval of the DES NADA's will result in an economic cost to society, I must know whether DES improves the efficiency of cattle and sheep production more than would the alternatives to which DES users would turn if DES were not available. To make my decision meaningful, however, I must also know to what extent other growth promotants will be available to replace DES and whether (and to what extent) such alternatives will be more expensive than DES.

The evidence in the record on the relative efficiency of DES and alternatives is not sufficiently clear for me to make any findings. A multitude of studies in the record (almost all submitted by the intervenors) show that DES (1) increases the rate of weight gain of steers and (2) decreases the amount of feed needed, and the amount of feed lot time needed, for fattening. It was, presumably, the demonstrated effectiveness of DES as a growth promotant that justified its continued approval after the 1962 amendments to the drug laws required that drugs be shown to be effective as well as safe. (There is no issue in this proceeding with respect to the evidence of DES's effectiveness except as that issue may affect the issue of benefits and (if benefits are relevant to safety) ultimately the issue of safety.) Thus, when compared to the use of no growth promotant at all, the use of DES has been shown to result in an economic benefit to cattle and sheep producers.

The more difficult question is whether, and to what extent, DES presents a significant economic benefit compared to the likely substitutes for it. The many substitute growth promotants mentioned in the record have been noted previously in section III(E)(1)(2)(c)(i). Tests included in the record comparing substitutes to DES provide sometimes

conflicting evidence on this question. Test conditions vary from actual conditions of use. No expert testimony was provided interpreting the results of these tests. For these reasons, I cannot make any findings on the basis of them.

Because the FDA is proposing to withdraw approval of the NADA's for Synovex-S and Synovex-H, I do not consider those drugs to be substitutes for DES. The tests comparing them to DES are thus not discussed here. Test results are reported for the following other potential substitutes:

Ralgro implant—In a test reported in 1975, a 15 mg DES implant was compared to a 36 mg Ralgro (resorcylic acid lactone) implant (PS–20). The Ralgro implant produced a slightly lower daily weight gain in a test with steers weighing from 309 to 352 kg, while requiring less feed per kilogram of gain than the 15 mg DES implant (id.). In a second test involving steers weighing 192 kg, the Ralgro implant caused slightly higher average daily gain than the DES implant and required slightly less food per kg of gain (id.).

In an unpublished report, a 36 mg Ralgro implant was found to result in a gain of about half the amount achieved with a 36 mg DES implant (PA–25). Essentially no improvement in cost of gain over controls was obtained with Ralgro (id.).

In a study reported in 1973, a 36mg Ralgro implant produced an average daily gain in steer calves slightly, but not significantly, greater than 10 mg oral DES and a 12 mg DES implant, with a feed-to-gain ratio essentially equivalent to that of the DES treatments (PS–12).

Estradiol 17-b—Estradiol 17-b, a natural estrogen, has been tested against various doses of DES under a variety of conditions (PS–12). In some of these, the Estradiol 17-b has been shown to be as good as or better than DES. In others it was not as good.

Melengestrol acetate (MGA)—Although neither DES nor MGA influenced the growth of steers and heifers during the hot summer months in feed lots in Arizona, a 24 mg DES implant increased the gains of steers significantly more than did MGA administered at the rate of 4 mg per animal daily (PS–44). On the other hand, heifers treated with MGA had significantly greater daily gains than control or DES treated heifers.

Dienestrol diacetate—A study reported in 1955 compared 10 mg DES with 10 mg dienestrol and found that dienestrol-fed steers gained "slightly less rapidly" than DES-fed steers, though their gains were significantly greater than the gains of the control animals (PS–19).

Testosterone Propionate—10 mg implants of this androgen in lambs produced average daily gains only slightly less good than those produced by 3 and 6 mg DES implants, but required more food per pound of gain than DES implants (PS–34).

Reserpine—This substance, when fed at 0.25 mg and 0.50 mg in lambs, produced average daily gains lower than DES implants or DES fed orally, with the higher amount of reserpine producing the worst results (PS–34). The feed per pound of gain was also increased over the DES treatments (id.).

Raising bulls instead of steers—As noted above in section III(E)(2)(c)(ii)(a), Dr. Donald R. Gill, a witness for the intervenors, testified concerning a suggestion that DES would be unnecessary if beef cattle were raised as bulls rather than steers. Dr. Gill testified that the problem with this suggestion was that bull feeding would require putting calves of 6 to 7 months of age on high grain rations. Apparently, under the present system such calves are grazed for from 6 months to a year before being taken to the feed lots and fed for the last 2 to 3 months of their life (see Tr. at 2013). Thus, according to Dr. Gill, shifting to the production of bulls would mean that grazing land presently used would cease to be useful and more grain would be consumed. Dr. Gill also noted that the consumption of grain, in a country where the government purchases grain surpluses, can be good one year and bad the next. He stated that on November 2, 1977, the date of cross-examination: "I was at a conference with USDA people last week, and with our surpluses it's becoming good again to use up grain" (Tr. at 2014). Dr. Gill further stated his opinion that the feeding of large groups of mature bulls (50 or more in 1 pen) presents a very serious management problem and will not work to the benefit of either producer or consumer (PA–32 at 2).

There is no reliable evidence in this record upon which to base conclusions about either the availability of substitutes for DES or the relative cost of such substitutes. Presumably, in the absence of supply problems, market forces would make substitutes more widely available if DES were banned. Economies of scale might bring prices of these substitutes down from their present levels. Alternatively, the increased demand might drive prices up if supplies were constrained. New products currently under development might also affect the economic consequences of a ban of DES. Nothing in this record provides a basis for any findings on these questions.

(ii) *How Great is the Benefit?* The calculations by the manufacturing parties and pro-DES intervenors of the actual economic effect of a ban of DES are, in each case, unsupported. In addition, these calculations appear to be based on the assumption that the alternative to DES is the use of no growth promotant at all. No other evidence in the record provides a basis for a realistic calculation of the "real world" economic effects, if any, on society of the withdrawal of approval of the DES NADA's.

Dr. Jukes is cited by the manufacturing parties as testifying that the economic benefit to the American economy of DES is some $800 million to $1 billion annually (Manufacturing Parties' Exceptions at 180). The testimony cited bases its computations upon phrases attributed to Senator Kennedy and Representative Fountain, computing the cost respectively as $4 to $5 per person per year and $3.85 per person per year (M–99 at 17). No evidence is presented that would support the per capita estimates.

Dr. Preston, a manufacturing parties' witness, testified that "various estimates indicate that $8–15 are returned for every dollar invested in the use of DES in cattle and sheep production" (M–124 at 4). Dr. Preston was very vague, on cross-examination, in explaining who made the estimates and how they were arrived at (Tr. at 1620–21). He did say that the savings was based upon feed efficiency and the overhead, interest, "death loss" and other components of cost saved by the decrease in the time in the feed lot necessary for DES-treated cattle (id.).

Intervenors' witness Dr. Gill estimated the value of the use of DES to feeders as $24 per head (PA–32 at 2). This figure was apparently calculated on the basis of savings in feed and feeding time resulting from the use of DES (see Tr. at 2008–09). Dr. Gill could not cite the studies upon which he relied for the proposition that pasture-fed steers treated with DES improved their gain by an average 22.46 percent. Although he offered to try to find these studies and produce them, they were not available for his cross-examination (Tr. at 2011) and have not been identified for the record.

An only slightly more helpful appraisal of the economic benefit of DES may be found in an inflation impact statement for the withdrawal of approval of the DES NADA's submitted by the Bureaus (G–115). The report is dated January 1976. It estimated the total cost impact of removing DES from

the market at $659 million during the first year (id. at 5). The bases for this evaluation are open to question.

It is estimated that feed lot producers of cattle will experience increased costs of $156 million (id.). Of this, approximately $4 million will be incurred by the producers of DES-implanted cattle as costs for changing to alternative estrogenic growth promotants (id.). The report stated that in 1974, 65 percent of fed steers received implants, of which 3.9 million of 10.9 million (approximately 36 percent) were using DES implants (id. at 4). The remainder were, it states using Synovex and Ralgro implants (id.). The assumption that those producers using DES implants would change over to the alternative estrogenic implants is based upon experience with the previous FDA ban of DES implants.

One hundred fifty-two million dollars in increased costs is allotted to the producers who use oral DES and represents the cost of increasing feed to provide the same amount of growth in untreated steers as would occcur with DES (id. at 4–5). The report states that 25 percent of the steers slaughtered in 1974 were receiving oral DES (id. at 3).

The assumption that producers feeding oral DES would switch to nonmedicated feed is also based upon experience with the previous ban of DES (id. at 4). The report notes, however, that the failure of producers to switch from oral DES to non-DES implants during the previous ban may be attributed to a shortage of supply of the non-DES implants (id. at 5). The allocation of cost—$152 million for the 25 percent of the steers that use DES orally and $4 million for the approximately 22 percent of steers that use DES implants (36 percent of 65 percent)—suggests that it would make economic sense for those using DES in feed simply to change over to non-DES implants. The report notes that in the opinion of a consulting animal scientist it would be no problem for a feed lot producer to make such a switch (id.).

The remainder of the estimated $659 million cost is allocated to an increase in the retail cost of meat by 2.2¢ per pound. This increased cost of $503 million is based upon an estimated decrease in the availability of meat. This estimate in turn is based, again, on no change-over from DES in feed to non-DES implants. It also assumes that meat producers do not, as they in fact do, decrease herd sizes when prices go down and increase herd sizes when they rise (cf. M–51 at 26).

(A witness for the intervenors, John W. Algeo, in fact testified concerning the "cattle cycle." He stated that at the time of his testimony, September 13, 1977, that cycle was coming to a turning point after years of over-supply and three years of liquidation (PA–29 at 4). He argued that lower production costs eventually mean lower meat costs but admitted that "this is at times hard to see due to the daily and cyclical market fluctuations" (id.). Mr. Algeo's testimony was withdrawn on the day on which he was to have been cross-examined (Tr. at 210), and I do not rely upon that testimony.)

An article by Mann and Paulsen, entitled "Economic Impact of Restricting Feed-Additives in Livestock and Poultry Production" (PA–22), apparently published in *Amer. J. Agr. Econ.* in February 1976, was submitted by intervenors. This article, using simulation techniques, attempted to predict the rise in wholesale prices that would be the result of bans of antibiotics and DES. This simulation takes into account the effect on prices of alternative meats should beef production be cut by the unavailability of DES. In a simulation dealing only with the unavailability of DES, the authors calculated that meat prices for beef, pork, broilers, and turkey would rise substantially and remain high for the five year period for which calculations were made.

The authors also performed a simulation, however, that takes into account the likelihood of technology developing replacements for DES and antibiotics. (The simulation assumed that it would take a year for replacement therapy to be available, though it acknowledged the present availability of Synovex and Ralgro.) In this assessment, the authors conclude that by the fourth year prices will actually fall below the first year baseline in each meat category after the ban of both antibiotics and DES (PA–22 at 51). This reduction in prices was predicted to result from the stimulation to supply provided by the increased prices during the ban, which would, as the cycle reached the point of slight over-supply, reduce prices.

Neither the authors of this report nor any other expert economist trained to forecast the likely effect of such actions as the withdrawal of approval of the DES NADA's was presented as a witness at the hearing. No attempt was made by any witness to analyze the real world economic effects of the lack of availability of DES and the availability of alternatives to it.

Moreover, the CAST Report contains a statement that would seem to contradict the manufacturing parties' position:

> A ban of DES at present would probably have little effect on the beef-cattle industry as long as substitutes, which have similar effects, remain available (Cothern, 1974, 1975, 1975a). Meanwhile, a ban on DES would permit the export of fed beef from the United States to countries such as Canada that now forbid its import because they ban DES and we do not.

(M–51 at 29.) The report also cites calculations of the estimated changes in wholesale prices of meats following withdrawal of approval of the DES NADA's with no substitutes being available. Because, however, there are substitutes, this information is of questionable relevance.

The CAST Report, in considering the possible effect of the removal of DES from the market "without replacement" on the availability of grains for export to developing countries, concludes that the "quantitative effects [of the ban of DES] would probably be too small to detect among the numerous other factors that influence prices of beef cattle and feed grains" (id. at 6).

This record simply lacks information sufficient to allow me to make any determination about the extent of the economic costs, if any, of the withdrawal of approval of the DES NADA's.

(iii) *Costs of Use of DES.* The Administrative Law Judge noted that a consideration of the possible economic benefits of DES must include consideration of the economic costs of such use (I.D. at 21). He cited the economic costs of "bulling" (id.). The term "bulling" or "riding" refers to steers mounting one another (I.D. at 21, n. 15). Although bulling occurs in feedlots without DES-implanted or fed cattle, the incidence of this activity increases where DES implants are used (Tr. at 2067). The only witness testifying on this subject, Dr. Flack, gave his opinion that DES feeding, as opposed to implantation, does not lead to increased bulling (Tr. at 2068).

The steers apparently can harm or kill one another during bulling. The record does not state the extent to which this activity increases, or the extent of harm to the cattle, when DES is administered. Nor does it provide information sufficient to be a basis for any conclusion about the economic costs associated with bulling.

The Administrative Law Judge also included in the economic costs of the use of DES a greater incidence of liver abscesses associated with that use. There is little information in the record about how much greater this incidence is in actual practice. The intervenors' Dr. Flack testified that livers of cattle are valued at approximately $2.50 per head

(Tr. at 2061). I cannot, however, on this record fairly estimate the cost to DES users and the economy resulting from the loss of livers abscessed because of use of DES.

One cost (or reduction in benefit) associated with DES-use that was not discussed by the Administrative Law Judge necessarily follows from the manufacturing parties' argument that DES-treated beef produces less marbling and, thus, a lower Department of Agriculture grade, than untreated beef. It is common knowledge that higher grade beef is more expensive than lower grade beef. If there is a significant difference, then meat producers pay a cost (or reduction in benefit) in lost profits resulting from use of DES.

(iv) *Conclusion As to Economic Benefits.* Again, the Administrative Law Judge's conclusion that the manufacturing parties have failed to show the economic benefit of DES is justified. Neither the manufacturing parties nor the intervenors provided information on the basis of which I can determine (1) the difference, if any, between the economic benefits of using DES and the economic benefits of using other growth promotants (or even what growth promotants are available), (2) the likely cost or savings from any changes in consumer selection of foods that might result from action with respect to DES, or (3) the costs that might be saved by the withdrawal of approval of the DES NADA's.

There is some credible evidence that the withdrawal of approval of the DES NADA's would cause little economic harm to the public and to the beef-cattle industry beyond the cost of transition from the use of DES to other products (cf. M–51 at 26). The transition cost itself may be lessened because of the way in which events have proceeded. The Administrative Law Judge's decision has put the industry, including the manufacturers of alternatives to DES, on notice that withdrawal of approval of the DES NADA's is likely. Presumably, the manufacturers of alternatives have been readying themselves to increase production when the withdrawal becomes final.

If there were no alternative growth promotants for beef and sheep, DES would provide some economic benefit, unquantifiable on this record, to society. In light of the availability of alternatives to DES, however, the manufacturing parties have not shown that the withdrawal of the DES NADA's would result in the loss to society of significant economic benefits.

Manufacturing parties argue that they have no "special burden to prove a point that the Bureaus have already conceded" in the inflation impact statement (Manufacturing Parties' Exceptions at 180). I do not agree that the Bureaus have conceded that the withdrawal of the DES NADA's will have the total economic impact stated in the inflation impact statement. That statement itself states that one of the pivotal assumptions upon which it relies, that producers using DES in feed will not switch to non-DES implants, may not be valid (G–115 at 5). In addition, that statement was a projection based on the economic situation in the beef cattle industry in 1976. As the Bureaus argue (Bureau's Brief at 144), conditions have changed since the issuance of that document. It would thus be unrealistic for me to rely upon the inflation impact statement as a projection of the economic costs of withdrawing approval of the DES NADA's.

Even accepting the manufacturing parties' position on this issue, I could not find that a saving of $659 million in the first year after withdrawal (projected by the impact statement) outweighs the risk of cancer associated with the continued use of DES. Even the manufacturing parties' Dr. Jukes stated his agreement with the proposition that no saving in meat prices can justify a real risk of cancer in the food Americans eat (Tr. at 2183–84). Some would argue that this amount of money, if put, for example, into cancer research, would result in a saving of more lives than would the ban of DES (see, e.g., M–99 at 17). There is, however, no showing that there is any relationship between the alleged savings of costs because of the use of DES and the funding of cancer research. In fact, there is clearly no such relationship.

(F) Summary of Safety Clause Issue

Evidence in the record from radiotracer studies and the Department of Agriculture residue monitoring program provides independent bases for the conclusion that approved uses the DES result in residues of DES and/or its conjugates in edible tissues of treated animals (see section III(B)). Animal and human cancer data demonstrate that DES is a carcinogen, and that there is no identifiable no-effect level for its carcinogenicity (section III(D)(1) and (2)). Evidence in the record raises but fails to resolve serious questios about the potential teratogenicity and mutagenicity of DES, and there is no demonstrated no-effect level for DES for these adverse effects (section III(D)(3)). Because the conjugates of molecules often retain the characteristics of the unconjugated molecule, and because conjugates of DES hydrolyze to DES in the human body, safety problems with DES itself must also be attributed to DES conjugates (section III(C)).

Risk-benefit analysis is not appropriate in determining the safety of an animal drug that poses a risk to humans (section III(E)(1)). Such an analysis has been attempted here nevertheless (section III(E)(2)). The proponents of the use of DES have the burden of showing that the benefits of DES outweigh its risks (id.). They have not, in this record, provided an adequate basis for determining either the risks of DES or the benefits, if any, that it provides to society (id.).

Withdrawal of approval of the DES NADA's is thus required on the basis of the so-called "safety clause" of 21 U.S.C. 360b(e)(1)(B) (as well as on the basis of the Delaney Clause discussed in section II of the Decision).

IV. Liver Discard as an Alternative Condition of Use

The manufacturing parties note (Manufacturing Parties' Exceptions at 186) that the Court of Appeals in *Hess & Clark* stated that "the FDA might restrict such consumption [of any DES residue] by a ban on sale of liver, the only food material in which any residues have been detected" (footnote omitted), 495 F. 2d at 994. As discussed above (section III(B)(1)) with respect to the manufacturing parties' contention that the NADA's for DES as a feed additive should be judged as if they provided for 14-day withdrawal periods, the statute is clear that I must consider the conditions of use that were originally approved. Thus, a change in conditions of use to require liver discard would be proper only if the manufacturing parties had sought to amend their NADA's.

In seeking such an amendment, the applicants would have the burden of showing their product to be safe in the first instance. In a withdrawal proceeding, an applicant's interest in the status quo outweighs the public interest to the extent that the Bureaus seeking withdrawal have the initial burden, discussed above, of coming forward with evidence warranting that withdrawal. When an applicant seeks approval for a change in the NADA, that burden on the Bureaus no longer exists.

I have, however, considered the question whether approval of the DES NADA's would still have to be withdrawn if they required as they now do not, the discard of all livers.

The *Hess & Clark* Court's understanding that livers were the only food material in which DES residues had been detected is not correct. DES residues have been reported by the

Department of Agriculture only in livers (G–58 at 2). That Department, however, only analyzes livers (G–94 at 3). As noted in section III(B)(2) of this Decision, DES residues were found in edible tissues other than liver, e.g., kidneys and tongues, in radio-tracer studies (see G–2; G–5; G–76 at 5; cf. G–79) of both feeding and implantation of DES.

The manufacturing parties, however, focus on the question of whether DES residues have been found in muscle tissues. As discussed above in section III(B)(2), radioactivity that may be attributable to DES residues has been found in the muscle tissue of steers 10 days after dosing with radiolabeled DES (G–2 at 1190, Table 4) and 120 days after implantation with radiolabeled DES (G–1 at 4; G–5 at 535, Table 2). The manufacturing parties' criticisms of these results, which are at very low levels, are discussed above (see section III(B)(2)).

More important than these findings is the fact that in the muscle of animals tested at less than approved withdrawal times, DES residues were observed in amounts significantly less than those found in the animals' livers. In light of that fact, I conclude that evidence that DES has been detected after use of DES animal drugs under their approved conditions of use in cattle's livers (and other organs) is an indication that DES exists, in smaller (perhaps undetectable) amounts, in muscle tissue. See also M–63 at 261, citing Goldhammer, G. S., Government Operations—Part I (1971) at 70 for the proposition that the concentration of DES in liver is ten times that in beef muscle.

I find that the record supports the conclusion that use of DES results in DES residues in edible tissues other than liver. It follows from this finding that it has been shown that use of the DES animal drugs, even with the restriction that the livers of DES-treated animals (Or that any combination of the edible tissues of such animals) be discarded, has not been shown to be safe. Therefore, even if the DES NADA's contained the liver-discard condition of use, approval would be withdrawn pursuant to the "safety clause" of 21 U.S.C. 360(e)(1)(B).

My analysis of the Delaney Clause issue would also not change. The approved or proposed analytical methods would be no more acceptable if the NADA's provided for liver discard. On that basis, withdrawal would still be required by the statute.

(The intervenors assert that liver tissues containing substantial quantities of DES are not "edible tissues" within the meaning of the Wholesome Meat Act, 21 U.S.C. 601 et seq. (Intervenors' Exceptions at 2). It is unclear what point they seek to make. If they are arguing that USDA will automatically remove from the market tissues with DES residues, I reject that argument. As discussed above (section II(A)), there is no analytical method available by which USDA could assure that meat does not contain DES residues at levels not shown to be safe. If they are arguing that no method can ever detect DES residues in edible tissues, see 21 U.S.C. 360b(d)(1)(H), because any tissue that contains a residue is not edible, I reject that argument as absurd.)

V. Need for an Environmental Impact Statement

The National Environmental Policy Act, 42 U.S.C. 4322(c), requires the preparation of an environmental impact statement for "major Federal actions significantly affecting the quality of the human environment, * * *" The Bureaus, in an "environmental impact analysis report and assessment," issued in October of 1976 (prior to issuance of the notice of hearing), found that the ban of DES would not constitute an action "significantly affecting the quality of the human environment" (G–116). The Bureaus thus concluded that no detailed environmental impact statement need be prepared. The basis for the Bureaus' conclusion was the finding that meat producers will simply turn to available alternative growth promotants if DES is no longer available. The report refers specifically to estradiol benzoate plus testosterone propionate (Synovex-H), estradiol benzoate plus progesterone (Synovex-S), zeranol (Ralgro), melengestrol acetate (MGA), and monensin (Rumensin).

It is appropriate, under the statute, for an agency to determine that its proposed action does not create the kind of significant environmental impact that would justify a full environmental impact statement. That decision must be based upon a careful consideration of the question, including consideration of courses of action that are alternatives to the action proposed, *Trinity Episcopal School Corp.* v. *Romney*, 523 F.2d 88, 92–93 (2 Cir. 1975). The Bureaus' statement is quite detailed, has a bibliography listing 21 articles and books, and does consider the alternatives to the withdrawal of approval of the DES NADA's.

The most important finding of the report is, of course, that users of DES will predictably turn to alternative growth promotants. The report bases this conclusion on experience during the period when approval of the DES NADA's was withdrawn previously before being reinstated by court order. The report notes that the alternative drugs to which it refers are approved by the FDA for use. No one disputed, at the hearing, the Bureaus' assertion that alternatives are available.

Intervenors' witnesses did, however, raise questions about reliance upon the availability of two alternative growth promotants. First, an intervenors' witness noted that the FDA is seeking to withdraw approval of the Synovex products (PA–33 at 5). The problem posed by the proposed withdrawal of approval of the Synovex products is discussed above in the benefits section. The agency was not proposing to withdraw approval of these drugs at the time the Bureaus' decision that an environmental impact statement was unnecessary was made. Because alternative growth promotants such as Ralgro are still available, I conclude that the proposed action with respect to Synovex does not invalidate the decision that the withdrawal of approval of the DES NADA's will not significantly affect the quality of the human environment.

Another intervenors' witness argues that the fact that monensin can be used either concurrently with DES therapy or by itself means that monensin is not properly a replacement for DES (PA–31 at 6). The Bureaus do not contest the assertion that monensin is additive to DES treatment and that, for that reason, monensin should not be considered a substitute for DES for those now using the two drugs concurrently. As a practical matter, on the other hand, cattle feeders who are content to use only one growth promotant may well begin to use monensin when DES is banned.

The preparation of the environmental impact analysis report by the Bureaus before the hearing commenced was the correct procedure, see *Calvert Cliffs' Coordinating Committee* v. *Atomic Energy Commission*, 449 F.2d 1109, 1117–18 (D.C. Cir. 1971). The manufacturing parties argue that they were denied a fair hearing on the environmental impact issues because the Bureaus did not present a witness to stand cross-examination on the environmental impact analysis. The courts have not gone so far as to require that the authors of the analysis be presented for cross-examination. Rather, the requirement is that the analysis (or statement) be available so that the parties are "given the opportunity to cross-examine * * * witnesses in light of the statement." *Greene County Planning Board* v. *FPC*, 455 F.2d 412, 422, (2d Cir. 1972).

The manufacturing parties argue that the economic and public health effects of the ban of DES, discussed above, demonstrate that the ban would be a major federal action significantly affecting the quality of the human environment (Manufacturing Parties' Exceptions at 184). The manufacturing parties do not explain how loss of the claimed economic benefits of DES would constitute an effect on the quality of the human environment. The Bureaus' analysis did consider the effect that the ban would have on the availability of feed (G–116 at 11). The analysis did not consider the effect of the ban on human intake of fat.

An increase in fat intake is not an environmental effect to be considered in an environmental assessment. See *Calorie Control Council, Inc.* v. *DHEW*, No. 77–0776, slip op. at 5–6 (D. D.C. September 9, 1977), *remanded on other grounds* (D.C. Cir. September 22, 1978) (health effects of saccharin ban not cognizable under environmental law); cf. *Breckinridge* v. *Rumsfeld*, 537 F. 2d 864, 866 (6th Cir. 1976); *National Ass'n of Gov't Employees* v. *Rumsfeld*, 413 F. Supp. 1224, 1229 (D. D.C. 1976). In any case, the fat question is unusual enough that it is not logical that it would have been raised in the initial analysis. In fact, in light of the evidence in this record, I consider this issue as bordering on the frivolous. I conclude that the full discussion of the issue in this opinion satisfies the statute's intent that all environmental issues be considered before action of this type is taken.

The manufacturing parties point out that although the Administrative Law Judge found that the withdrawal of DES from the market would not significantly affect the quality of the human environmenmt, he did not discuss this issue specifically in his opinion. (The manufacturing parties themselves devote only two and a half of the 217 pages of their exceptions to this issue.) I have, however, considered carefully the possibility that the withdrawal of approval of the DES NADA's will affect the human environment. This discussion, together with the applicable segments of the risk/benefit analysis, constitutes my decision on this issue.

I conclude that withdrawal of approval of the DES NADA's will not significantly affect the quality of the human environment because DES will be replaced by alternative growth promotants. Therefore, the Bureaus' decision not to file a complete environmental impact statement for the withdrawal of approval of the DES NADA's was correct.

VI. Exceptions to Evidentiary Rulings

Both the manufacturing parties and the Bureaus have filed exceptions to certain evidentiary rulings by the Administrative Law Judge in the course of the hearing. In the interest of removing any possible cause for remand of this hearing from a reviewing court due to evidentiary rulings, I have considered those evidentiary submissions by the manufacturing parties that were excluded from the record, whether or not I have concluded that those exclusion were proper.

I have relied upon certain Bureaus' evidence that the manufacturing parties argue should be excluded. I have, however, reviewed the record carefully to determine whether reversal of any evidentiary ruling with respect to such evidence would change my decisions on the issued presented by this hearing. Thus, the following discussion considers, in each instance in which I uphold the refusal to exclude Bureaus' evidence, whether excluding that evidence would alter my conclusions in any respect. As will be apparent, even if all evidence that the manufacturing parties seek to exclude were in fact excluded from the administrative record, my decision of the issues presented would not change.

(A) *Manufacturing Parties' Exceptions.* The manufacturing parties have specifically excepted to certain exclusions of their evidence (Manufacturing Parties' Exemptions, Appendix C). I will, as did the manufacturing parties in their exceptions, review those rulings under the name of the witness, or the number of the exhibit, in question.

Direct testimony of Dr. Booth (M–40). The manufacturing parties except to the striking of a sentence from page 8 of Dr. Booth's testimony. That sentence was stricken neither in the October 20, 1977, order to which they refer nor during cross-examination. Although the sentence referred to appears on its face to be unobjectionable (and I have therefore, considered it), the manufacturing parties' failure to state in what context the decision to strike was made makes reversal of that decision inappropriate.

Direct testimony of Dr. Jensen (M–669). The manufacturing parties except to the exclusion of a statement by Dr. Jensen concerning a study dealing with estrogen receptors. A written report of the study was apparently prepared but not yet published and was not submitted to the record. The data upon which Dr. Jensen based his statements were not available for analysis by the Bureaus, and Dr. Jensen's report of those data is hearsay.

I find, however, that this testimony should have been admitted for what it is worth, and I therefore reverse the Administrative Law Judge's ruling on this issue.

Direct testimony of Dr. Kliman (M–110). The manufacturing parties except to the exclusion from evidence of pages 19 through 29 of Dr. Kliman's testimony. The Bureaus had sought the exclusion on the grounds that this testimony, which dealt specifically with the testimony of Bureaus' witnesses, was argumentative and, in some instances, irrelevant and without factual basis. The statements made in this part of Dr. Kiliman's testimony would more appropriately have been made in a brief. I find, however, that there is sufficient basis for this testimony to support its admission into evidence and I reverse the Administrative Law Judge's ruling with respect to the pages in question. I have discussed Dr. Kilman's testimony, where relevant, above.

Direct testimony of Dr. Tennent (M–132). The manufacturing parties except to the striking of the last sentence on page 7 of Dr. Tennent's testimony. The motion to strike this testimony was originally denied but was then, after cross-examination of Dr. Tennent, granted (Tr. at 1283). The testimony was stricken as hypothetical and not relevant to the proceeding. The statement stricken deals with a calculation for which Dr. Tennent admitted he did not have data (Tr. at 1282) and which was not directly related to the issues at hand. Although it is not clear why there was a need to strike this testimony, I do not find that striking to be error.

The manufacturing parties also except to the striking of a statement by Dr. Tennent concerning a procedure followed by Dr. Williams in attempting to identify radioactivity found in a radioisotope experiment. The first of the two sentences stricken states that Dr. Williams made a certain assumption. The Bureaus moved to strike this statement because Dr. Tennent had not shown a basis for concluding that the assumption had been made. The striking of that sentence appears to have been appropriate. However, the next sentence, which states: "This procedure was counterproductive so far as purification is concerned," is simply a statement of expert opinion on a relevant subject and should not have been stricken. I therefore reverse the Administrative Law Judge's ruling with respect to the latter sentence. I do not, however, consider Dr. Tennent's

testimony to be a basis for discounting the results Dr. Williams reported.

Direct testimony of Dr. C. R. Weaver (M–139). The manufacturing parties object to the striking after cross-examination (Tr. at 1520–21) of a statement by Dr. Weaver about the "apparent experimental design" of the Gass study. Dr. Weaver admitted on cross-examination that he based his testimony on a statement by Dr. Tennent, who was in turn reporting a statement by Dr. Gass (Tr. at 1518). It was within the Administrative Law Judge's discretion to find this double hearsay to be unworthy of admission into evidence in this proceeding, and his ruling is upheld with respect to those statements. The Administrative Law Judge also struck from the record a statement by Dr. Weaver about the usual procedure in a controlled experiment. This testimony is relevant only if Dr. Weaver's hearsay testimony about the experimental design of the Gass study remains in the record. Thus, the striking of this testimony was also appropriate.

The manufacturing parties object to the striking of two paragraphs (at pages 19 and 20 of M–139) that seek to incorporate the views of a Professor Mantel. I believe that a fairly liberal policy with respect to the receipt of hearsay is appropriate in a proceeding such as this one. One legitimate function of that rule, however, is to force the parties to present witnesses that they regard as important for cross-examination. If the manufacturing parties wished to rely upon the views of Professor Mantel, they had an obligation to present him as a witness for cross-examination. This testimony was properly stricken as hearsay.

Exhibits M–141 and M–142. The manufacturing parties object to the exclusion from evidence of affidavits of Drs. Nathan Mantel and David Salsburg. Because neither of these individuals was made available for cross-examination, the striking of their affidavits was entirely justified. (Although the manufacturing parties argue that this ruling by the Administrative Law Judge is inconsistent with other rulings that permitted witnesses to refer to statements of other experts, they provide no examples of such "other rulings.")

Exhibit M–148a. This exhibit purports to list reported residue findings for animal drugs other than DES. The striking of this exhibit is consistent with the agency's, and the Administrative Law Judge's, established position that an administrative hearing on one product is not a proper forum for an argument that that product is being treated differently than other products. This position has been recently upheld by the United States Court of Appeals for the District of Columbia Circuit, *Edison Pharmaceutical Co., Inc.* v. *FDA*, No. 77–1636, slip op. at 23 (D.C. Cir. March 21, 1979).

In any case, as discussed in section III(B)(3) of this Decision, the evidence with respect to the regulatory treatment of the residues of other drugs is irrelevant to the evidence with respect to DES because the residue findings are not comparable. With respect to other drugs, residues should be detectable by the approved methods at any level above a computed "safe" or "virtually safe" ("no residue") dosage. Since no "safe" or "virtually safe" dosage for DES can be ascertained, there is no evidence of the number of residues existing in edible meat products above that dosage level for DES. Certainly the Department of Agriculture findings, which at best provide evidence of the number of residues above 0.5 ppb DES, are not comparable to the residue figures for other drugs.

Surrebuttal testimony of Dr. Jensen (M–203) and referenced papers (M–204–208). Briefs to the Administrative Law Judge were due to be filed on March 30, 1978. On March 3, 1978, the manufacturing parties presented the purported surrebuttal testimony of Dr. Jensen together with a number of papers that had not yet been made part of the administrative record. The Administrative Law Judge reviewed this new evidence and concluded correctly that it was not proper surrebuttal. The arguments made by Dr. Jensen, in almost all instances, would more appropriately have been made in the final brief of the parties. In fact, Dr. Jensen's testimony has been included in the manufacturing parties' brief (Manufacturing Parties' Exceptions, Appendix B).

The Administrative Law Judge's decision to exclude this evidence on the ground that it was not proper surrebuttal was correct. Surrebuttal is justified only by a showing of the necessity to respond to unanticipated issues raised during rebuttal. It is clearly not appropriate for the manufacturing parties to seek to introduce as surrebuttal new evidence that could have been produced earlier in the hearing and would have been subjected to the scrutiny of the witnesses for all parties. Since there was no showing that exhibits M–204–208 were not available earlier in the proceeding (or that the issues to which they are relevant were not raised earlier in the proceeding), the Administrative Law Judge's decision with respect to these documents was clearly justified.

The manufacturing parties' desire to have the last word (and perhaps to delay the completion of the hearing, since acceptance of surrebuttal testimony would have led to further cross-examination) is understandable. Administrative hearings have to end sometime, however, and the conclusion of this hearing prior to the submission of the manufacturing parties' purported surrebuttal evidence was appropriate.

Exhibit M–209. As discussed below, the Administrative Law Judge allowed the Bureaus to submit into evidence an interim report (G–192) of the "Chicago study", discussed above (see section III(D)(2)(b) above). In their opposition to admission of this document, the manufacturing parties submitted a statement by Dr. Herbst, who had been a witness for the Bureaus. Dr. Herbst, in this statement, gave his opinion that the report was not evidence of carcinogenicity of DES in humans. The exhibit (G–192) was nevertheless admitted and, on March 20, 1978, (ten days before final briefs were due), the manufacturing parties moved Dr. Herbst's statement into evidence (Record No. 373). On March 24, the Administrative Law Judge denied the motion for admission of Dr. Herbst's statement.

Exhibit G–192 was an update of a study about which all parties had had an opportunity to comment. Neither the Bureaus nor the manufacturing parties were given an opportunity to present testimony concerning the update. Accepting testimony from either side on this report would have required another round of cross-examination.

The Administrative Law Judge noted that, by the terms of Dr. Herbst's statement, Dr. Herbst and the other researchers working on the "Chicago study" had completed an analysis of the study. They were not, however, willing to submit that analysis to the administrative record before the publication of the analysis in April. The failure to admit, at that late date in the proceeding, the partial, conclusory evaluation of the study that was proffered is not error. The manufacturing parties were free to comment upon the information presented by the report and have done so in their briefs. (As noted above, I have considered Dr. Herbst's statement in any case.)

The manufacturing parties also objected to the admission into evidence of certain testimony and exhibits presented by the Bureaus.

Direct testimony of Dr. Bixler (G–11). One sentence from this testimony is objected to because it uses the phrase "the livestock producer may think he is

feeding his animals a withdrawal (nonmedicated) feed" (G–11 at 2). The manufacturing parties argue that this testimony "purports to probe the mental processes of 'the livestock producer,'" (Manufacturing Parties' Exceptions, Appendix C at 13). Since the rest of this statement explains Dr. Bixler's view of the likelihood of unintentional DES drug carryover, this testimony is properly admissible. I have not, however, relied upon Dr. Bixler's testimony in this Decision.

Cross-examination of Dr. Bixler. The manufacturing parties object to a statement made by Dr. Bixler on cross-examination in which he testified that it was possible that animals implanted with DES might also be inadvertently fed feed containing DES. The Administrative Law Judge correctly denied a motion to strike this statement; he thought the question on cross-examination was unnecessary and that the answer was obvious. He noted that counsel for the manufacturing parties had, in his objection to the question, pointed out that anything was possible.

Dr. Bixler also stated that "farmers have admitted that they have fed DES feed in conjunction with implanting" (Tr. at 571). This statement is hereby stricken as hearsay.

Exhibit G–47. The manufacturing parties move to strike this document, entitled "Survey of Compounds Which Have Been Tested for Carcinogenic Activity." This is a government publication briefly summarizing test results with respect to the carcinogenic activity of various substances. An administrative law judge is not bound by the Federal Rules of Evidence, though Judge Davidson sought to apply them to the extent reasonable in this proceeding. The Administrative Law Judge concluded that G–47 was admissible, even though hearsay, either because it was a public record or report or because its admission otherwise served the purposes of justice; see Rule 803, Fed. R. Evid.

The admission of this exhibit might conceivably have been improper if it had been intended to show the results of a particular study about which there was an active dispute and if that study had not been produced. Here, however, that was not the case. The studies specifically relied upon by the Bureaus were produced. This exhibit was proffered merely to demonstrate that DES is carcinogenic. The Administrative Law Judge's decision not to strike this document was proper. There is sufficient evidence in the record showing DES to be a carcinogen in animals so that, if G–47 had been excluded from evidence, my findings would not change on any issue.

Direct testimony of Dr. Highman (G–54). The manufacturing parties object to the entire direct testimony of Dr. Highman. Dr. Highman reported on incomplete results of the NCTR DES animal study. The manufacturing parties also submitted testimony with respect to incomplete reports of the results of this study (see section III(D)(2)(a) of this Decision). The question of how to deal with ongoing studies in an administrative hearing is a difficult one. I have concluded that it is not appropriate to rely, in an administrative hearing, upon incomplete reports of results of a study of this type. Although the technical question of whether this testimony is admissible is perhaps a close one, in light of the fact that I have assigned no weight to this evidence (see section III(D)(2)(a) of this Decision), I hold that this testimony should be excluded.

Direct testimony of Dr. Kokoski (G–57). The manufacturing parties seek to strike certain testimony of Dr. Kokoski setting out what he and the Bureau of Foods' Division of Toxicology consider necessary to show the safety of a substance. The manufacturing parties' objection to this testimony is that it represents the views not of the individual witness but of the division of the Bureau. Since, however, Dr. Kokoski stated that this testimony on these subjects was in fact a statement of the criteria he would use in evaluating the safety of a substance (Tr. at 1018–19), it is apparent that this testimony is properly admissible. I conclude that the exclusion of his testimony on this subject would not have led me to a different decision with respect to the safety of DES.

Cross-examination of Dr. Kokoski. The manufacturing parties refer to a response to a question asked Dr. Kokoski on cross-examination in which Dr. Kokoski stated his opinion that the "law does not provide for establishing a safe tolerance for an agent which is shown to induce cancer" (Tr. at 1045). The manufacturing parties moved to strike this sentence, apparently on the grounds, urged at the time of cross-examination, that Dr. Kokoski is not qualified to give an opinion on a legal question. I fail to see why any time is wasted by either making this objection or appealing the ruling denying it. It would seem an obvious matter that Dr. Kokoski's opinion on a legal matter will be given no weight. Because the legal opinion was not within Dr. Kokoski's expertise, however, the Administrative Law Judge's ruling on this issue is reversed.

The manufacturing parties also object to three answers by Dr. Kokoski to questions on redirect examination (Tr. at 10, 48–49). In this testimony Dr. Kokoski stated that Exhibit G–24 refers to drugs in general, though its primary thrust deals with carcinogenic drugs. The manufacturing parties then moved to strike this redirect examination as not having been covered on cross-examination. The Administrative Law Judge denied the motion to strike on the ground that whether or not the witness was correct in his appraisal of the exhibit was immaterial, because the exhibit was in evidence (and could thus be evaluated on its own merits). He stated, "I do not know what you are fussing about" (Tr. at 1049). I concur in the Administrative Law Judge's comment upon the frivolousness of this motion. It is unclear whether the Administrative Law Judge ruled upon the issue of whether the testimony in question was proper redirect examination. As I can find nothing in the cross-examination of Dr. Kokoski that deals with the subject of his redirect, I must reverse the Administrative Law Judge's denial of this motion.

Direct testimony of Dr. Levy (G–58). The manufacturing parties ask that this entire testimony be stricken because Dr. Levy did not have personal knowledge of the factual data upon which he based his statistical calculations (discussed above in section III(B)(3) of this Decision). Dr. Levy's testimony can be accepted, at the very least, as demonstrating the fact that a relatively small number of detected residues represent a larger number of residues among all animals treated. (The manufacturing parties do not object to this treatment of the testimony, Tr. at 738.)

Dr. Levy testified that the figures he utilized in this testimony were government figures provided by the United States Department of Agriculture. The manufacturing parties provided no basis for suspicion that these figures are not correct. In an administrative hearing of this type, struct adherence to the evidentiary rules of courtrooms is neither required nor efficient. If there were any reason to believe that USDA had in fact not found the residues reported by Dr. Levy or if the difference of a few residue detections more or less would make a difference in my ultimate decision, there would be more reason to require technical proof that the figures to which Dr. Levy testified were correct. Because neither of these reasons, nor any other reason of which I am aware, requires

dismissal of Dr. Levy's testimony, I have relied upon it and hold that the denial of the motion to strike this testimony was appropriate.

I have considered whether exclusion of Dr. Levy's testimony would require reversal of any of my findings in this proceeding. FDA Establishment Investigation Reports have been submitted to the record (as G–89) that show FDA investigations of USDA DES residue findings (see also G–139, G–140). Thus, there would be evidence of such findings—upon which I would base the conclusion that USDA findings show that DES use results in DES residues in edible tissues—even were Dr. Levy's testimony excluded.

Direct testimony of Dr. Rodricks (G–72). The manufacturing parties move to strike Dr. Rodricks' statement that, because the USDA monitoring program was utilizing a method with a lowest level of measurement above the level that would be considered adequate for DES, it must be concluded that a far higher residue occurrence rate would be observed if a method with a lower level of measurement were utilized by the monitoring program (G–72 at 6). The manufacturing parties argue that this conclusion is speculative and without factual basis in the record. However, Dr. Rodricks was an expert witness, and the conclusion is appropriately based upon his expertise. (Indeed, the conclusion he voiced is self-evident to one with basic scientific knowledge about the occurrence of residues.)

The manufacturing parties also object to the admission into evidence of a number of statements by Dr. Rodricks (id. at 7–10) that they consider to be "argumentative, hearsay, and to a large extent not based upon evidence of record." I have reviewed the statements objected to and find the manufacturing parties' objections to them to be unfounded.

Direct testimony of Dr. Saffiotti (G–80). The manufacturing parties move to strike the first seven pages of Dr. Saffiotti's eight page written direct testimony on the grounds that it set out procedures for determining whether chemical carcinogens are safe and that Dr. Saffiotti was unable to relate DES to chemical carcinogens. The manufacturing parties' argument is that DES is simply another estrogen and thus not a chemical carcinogen. As discussed in some detail above (section III(D)(1)), I find that DES is not simply another estrogen and may have some properties of chemical carcinogens. Thus, Dr. Saffiotti's testimony is relevant to DES, and the refusal to strike this testimony was justified. (The first one and one quarter pages of the testimony contains, at any rate, a description of Dr. Saffiotti's qualifications and would not, even if the manufacturing parties' theory had validity, be stricken.)

The manufacturing parties also object to a statement by Dr. Saffiotti that: "It is clear that DES is a cancer-causing agent in animals and in humans," and to a subsequent statement that a publication containing summaries of experimental and epidemiological data supports that statement (G–80 at 7). The manufacturing parties argue that they were unable to cross-examine Dr. Saffiotti fairly on his conclusion that DES is a cancer-causing agent because they had not been provided with copies of all of the reports summarized in the publication referred to. However, Dr. Saffiotti's expertise in this area is clear (G–80 at 1–2; G–80a; G–80b), and he is qualified to give the opinion, based upon literature upon which he reasonably relies in forming opinions of this type, that DES is a carcinogen (cf. Rule 703, Fed. R. Evid.; *McCormick on Evidence* (2d Ed. 1972) at 36). Thus, his conclusion on that point would be admissible whether or not he had stated that data supporting his testimony were summarized anywhere.

The statement that such summaries exist seems to be straightforward and need not be stricken. A study in the record showing DES to be a carcinogen, such as the Gass study, is, of course, given more weight than the statement of an expert, unsupported by submitted evidence, that DES is a cancer-causing agent. The latter statement is, however, relevant evidence and should be considered as such (id.). I note that there is ample evidence of the carcinogenicity of DES in the record so that, if Dr. Saffiotti's testimony were excluded, no finding I have made in this proceeding would change.

Exhibits G–139 and G–140. These exhibits contained reports from the Department of Agriculture to the FDA about recent findings of DES residues. It was established on the record that these memoranda were prepared and transmitted in the normal course of government business (Tr. at 1183–84). As such, these documents are properly admissible in a Food and Drug Administration administrative hearing. Even if they did not, as they appear to do, come within a recognized exception to the Federal Rules of Evidence hearsay rule, Rule 803(8)(B), Fed. R. Evid., it would be necessary for the orderly conduct of Food and Drug Administration administrative hearings to admit this type of evidence unless a reasonable basis for believing that the evidence was not correct had been proffered. No such basis was proffered here. I note that these documents were only cumulative of other evidence of USDA residue findings and that exclusion of them would not, therefore, change my finding on any issue.

Direct testimony of Dr. Shimkin (G–90). The manufacturing parties object to the testimony by Dr. Shimkin to the effect that it is not possible to conclude that any level of DES residues can be shown to be safe for human consumption. Though the manufacturing parties argue that this is a legal conclusion, I do not share that characterization. The statement objected to is an appropriate conclusion for an expert witness. Even under the Federal Rules of Evidence, an expert witness may give his opinion on the ultimate issue to be decided by the factfinder. Rule 704, Fed. R. Evid. This testimony is not, however, an essential basis for any finding that I have made.

Direct testimony of Ms. Weissinger (G–95). The manufacturing parties object to testimony by Ms. Weissinger about a study of the breakdown of DES conjugates in humans. This study was an outgrowth of work she had done on the subject in animals (see G–95; Tr. at 827–28). Ms. Weissinger was not a party to the actual performance of the tests in humans. The manufacturing parties object to her testimony about the study on that ground. However, the record is replete with testimony by persons shown to have expertise about studies that they did not perform (see, for example, my discussion of the conflicting expert interpretations of the Gass study in section III(D)(2)(a)). Ms. Weissinger has significant expertise in the performance and evaluation of this general type of study (G–95 at 1–2; G–95a), and there is thus no valid objection to her testimony concerning this study, a report of which is part of the record (G–97). Because the study itself was part of the record of this proceeding, I find that I would reach the same conclusions about the significance of this study even were Ms. Weissinger's testimony excluded.

Submission of Dr. Williams (G–102). The manufacturing parties object to Dr. Williams' statement that "[t]here appears to be no reasonable doubt that DES conjugate(s) are present in liver 120 days after implantation of ^{14}C–DES" (G–102: Comments on the Vineland Laboratories Submission at 1). The manufacturing parties' objection to this statement as being beyond the expertise of the witness, speculation and without proper foundation, is totally without merit. Dr. Williams has been shown to be an expert in this area (G–99 at 1; G–

99a; G–99b). A second sentence in the same paragraph, in which Dr. Williams gives his opinion as to whether a conjugate constitutes a residue of DES, is less clearly within Dr. Williams' area of expertise. The question is simply one of semantics. Whether or not conjugates found in animal tissues as the result of the use of DES are characterized as "residues" is of no significance in this hearing. Although I have not relied upon Dr. Williams' testimony on this issue, I conclude that the Administrative Law Judge's refusal to strike it was proper.

The manufacturing parties object to a statement by Dr. Williams that an estrogen conjugate is known to give rise to high circulating plasma levels of free estrogen in humans after oral administration. Dr. Williams cited a private communication from another scientist for this proposition (G–102: Comments on the Vineland Laboratories Submission at 2). The manufacturing parties were not given an opportunity to examine the data (or a report of the study) about which Dr. Williams testified, and Dr. Williams' statement is hearsay. I have concluded, however, that this statement like that of Dr. Jensen in M–69, discussed at the beginning of this section, should have been admitted for what it was worth. I have, however, not relied upon this statement.

The manufacturing parties also object to a further statement by Dr. Williams that he feels that "it is most probable that conjugated DES occurring in animal tissues will give rise to free DES after ingestion by humans" (id.). Contrary to the manufacturing parties' assertion, this statement is not beyond the expertise of the witness, does not constitute hearsay, and is an appropriate expression of an expert's opinion. (Dr. Williams cited bases for this opinion other than the hearsay statement discussed above (id.). In any case, that information would be a permissible basis for the formation of his opinion, rule 703, Fed. R. Evid.) Even were Dr. Williams' testimony excluded, other evidence in the record (see section III(C) of this Decision) would support the conclusion, discussed above, that I have drawn on this issue.

Exhibit G–137. The manufacturing parties object to the admission of this summary of the results of FDA investigations of DES residues. Apparently the manufacturing parties at one time thought this document was admissible, as they submitted it themselves (*M–27*). Nevertheless, there does not appear to be a clear explanation in the record of how this document was prepared. Nor is there any clear showing that this is a document prepared in the normal course of government business, though its format would suggest that it is. If the document summarized only establishment inspection reports that were submitted to the record, it might be admissible as a shorthand summary of those documents. However, some of the establishment inspection reports noted in the summary were not provided to the record. It appears that this document should have been stricken from evidence and I reverse the Administrative Law Judge's decision not to strike this document. I have disregarded the document in reaching my decision.

Exhibit G–192. This exhibit is the interim report of the Chicago study discussed above. The manufacturing parties' basic objection to this document is that it was submitted after the hearing was, in effect, completed and that the manufacturing parties were not provided a chance to present testimony analyzing the document. The Bureaus were not, however, given an opportunity to present testimony analyzing this document either. The manufacturing parties treat this document as if it were testimony as to which rebuttal evidence would be proper. The document, however, constitutes only data from which all parties can draw whatever conclusions appear to be appropriate.

Since this document was not available prior to the hearing itself, its admission after it became available was proper. Because I have based no conclusions on this document—see, e.g., discussion of human carcinogenicity data in section III(D)(2)(b)—the manufacturing parties are not, in any case, prejudiced by its admission.

(B) Bureaus' Exceptions

The Bureaus except only to the exclusion from evidence of certain statements that they regard as the opinions of experts on ultimate issues. Although I have not relied on any such statements, I regard the exclusion of expert testimony on the ground that it involves an opinion on the ultimate issue as inappropriate. The common law rule against such testimony was designed to protect fact-finding juries. Certainly here neither the Administrative Law Judge nor I am likely to be unduly swayed by any expert's opinion on an ultimate issue. The common law rule has, in any case, been changed for federal courts. Rule 704, Fed. R. Evid.

VII. Effective Date

The risk associated with continued use of the DES animal drugs is, though unquantifiable, significant. For that reason I do not believe that a substantial delay of the effective date of my decision is appropriate. Certainly no such delay would be proper without a clear showing that an early effective date would cause economic disruption in the meat production industry.

It is also true, however, that in a complex set of activities such as the manufacture, shipment, and use of animal drugs involving many economic units in different parts of the country, it is not feasible to terminate operations with a widely used drug immediately. Moreover, although for several years there have been clear signals that the continued approval of DES was in jeopardy (particularly, the Administrative Law Judge's decision in September, 1978), nevertheless there are legitimate reliance interests on the part of animal producers who, during the period while DES was approved, have administered it to animals that they will be bringing to slaughter in coming months. Those reliance interests deserve some equitable consideration.

I have concluded, therefore, that this decision will become effective in 14 days (on July 13, 1979) with respect to the manufacture of DES animal drugs and the shipment of DES animal drugs by anyone (including manufacturers, wholesalers, jobbers, and other middlemen or persons acting as middlemen). That effective date is intended to allow a fair and reasonable period (but no more than a fair and reasonable period) to bring the production and shipment of these products to an end. Petitions for stay of this effective date may be submitted pursuant to 21 CFR 12.139, 10.35; and arguments contained in such petitions will be considered expeditiously. Submission of such petitions will not, however, automatically stay this effective date.

I am also delaying the effective date of this action 21 days (until July 20, 1979) with respect to the administration of DES animal drugs to animals (in any form whether as an additive to feed or as an implant) and the manufacture, shipment, and use of feed containing DES. This effective date is intended to allow a fair and reasonable period (but not more than a fair and reasonable period) to bring these activities to an end. A somewhat longer period is allowed for bringing these activities to an end than is being allowed to terminate the manufacture and shipment of DES drugs. The reason for this difference is that the activities relating to the use of DES in feed or in animals involve many more economic units, some of which are small and may not

learn of this decision immediately. I have set this second effective date in the expectation that a petition or petitions for stay of this action will be received by the FDA prior to the end of the 21 day period. See 21 CFR 12.139; 10.35. Receipt of such petitions will automatically stay the effect of this decision with respect to the activities and persons covered by this paragraph for another period of 14 days (August 3, 1979). If petitions are received within 21 days, either they will be ruled upon before the end of the additional 14 day period or that period will be extended pending a ruling on the request for stay. I recognize that 21 days is a relatively short time within which to prepare the necessary papers. I also believe, however, that it is sufficient time; and I am concerned about the risk to the public from any continued use of DES animal drugs.

This Decision will not be effective with respect to edible products of animals treated with DES animal drugs when the treatment of the animals was before the effective date for use of the drug. Any added treatment of such animals with DES after the effective date (including the continuation of feeding with DES-treated feed begun before the effective date) will, however, make the meat from the treated animals adulterated within the meaning of the Federal Food, Drug, and Cosmetic Act; see discussion below. Implants inserted before the effective date will not be effected by this Decision even if they continue to operate after the effective date; no new or additional implants may be inserted, however, after the effective date.

I will first describe the legal consequences that will flow from my decision to withdraw approval of these NADA's on the dates that this decision becomes effective. I will then discuss the options that may be available to the agency if it finds that any further stay is appropriate. Finally, I will outline the data that must be submitted to support any petition for a further stay of this action.

The animal drugs themselves will, upon withdrawal of approval of the NADA's that cover them, be deemed, pursuant to 21 U.S.C. 360b(a), to be "unsafe" within the meaning of 21 U.S.C. 351(a)(5). Thus, pursuant to the latter section, these drugs will be "adulterated".

The withdrawal of approval of the NADA's will also mean that, pursuant to 21 U.S.C. 360b(a), DES will be deemed unsafe within the meaning of 21 U.S.C. 342(a)(2)(D). Pursuant to the latter section, any food containing DES will be deemed adulterated. Thus, animal feed containing DES and the edible products of animals treated with DES will be adulterated food within the meaning of the Federal Food, Drug, and Cosmetic Act.

The following acts with respect to adulterated drugs and adulterated foods (and thus with respect to DES, animal feed containing DES, and edible products of animals that have been treated with DES) are violations of federal law:

1. The act of, or causing the act of, the introduction or delivery for introduction into interstate commerce of such drugs or foods, 21 U.S.C. 331(a).
2. The act of, or causing the act of, receipt in interstate commerce of such drugs or foods or the delivery or proffered delivery of such drugs or foods, 21 U.S.C. 331(c).
3. The act of, or causing the act of, manufacture of such drugs or foods within the District of Columbia or any other federal territory, 21 U.S.C. 331(g).
4. The manufacture or doing of any other act with respect to a product if that act is done while the product is held for sale after shipment in interstate commerce and results in the adulteration of the product, 21 U.S.C. 331(k).

I interpret the latter provision as prohibiting the manufacture of DES, the mixing of DES with feed, and the treating of animals intended for food with DES when either the DES, its components, the feed, or the animals involved have crossed a state line.

If the FDA finds that a further stay of the effective date of this action is appropriate, several options suggest themselves. The decision might be stayed until judicial review of it has been completed. I do not regard that possibility as likely. The risk of use of DES is significant, and I believe that my decision is correct and will be upheld.

The agency could allow all existing stocks of DES to be used up. Alternatively, the agency could allow all existing stocks held by cattle producers and feed lots to be used up, but refuse to stay this decision as to stocks of DES that are now held by manufacturers or middlemen. Another alternative would be to stay the decision with respect to feed with which DES has already been mixed, but to deny a stay as to unused DES implants and DES drugs not yet mixed with feed.

I do not believe that I can make a decision adopting any of the alternatives listed without knowledge of how much DES is not available on the market, in what forms, and in whose hands that DES is. Cf. *Environmental Defense Fund, Inc.* v. *Environmental Protection Agency*, 510 F.2d 1292, 1306 (D.C. Cir. 1975).

Petitions for stay of the effective date of my decision should be submitted in the format prescribed by 21 CFR 10.35. They should identify the type of stay requested. The agency has no intention of allowing existing stocks of DES to be used up if it is apparent that manufacturers, cattle producers, or others have been stockpiling unusually large quantities of DES against just such a decision. The following information should be submitted in support of any petition:

1. The amount of existing stocks of DES held by manufacturing parties;
2. The amount of existing stocks of DES held by cattle producers and feed lots;
3. The amount of existing stocks of DES held by middle men, carriers, and other persons.
4. The time that it is estimated would be required to use up any presently existing stocks of DES (a) held by manufacturing parties, and (b) held by others.
5. A comparison of the amount of DES produced from January 1 through June 30, 1979, with the amount produced during the comparable period in 1976, 1977 and 1978.
6. A statement of the amount of DES produced between June 29, 1974, and July 13, 1979 (the effective date of this decision with respect to manufacture of DES animal drugs).
7. An explanation of the petitioner's reasons for believing that a stay would cause economic disruption in the cattle producing industries, accompanied by factual data supporting that explanation.
8. An explanation of the legal basis upon which the petitioner relies in requesting the type of stay requested.
9. Any other reason that the petitioner believes justifies a total or partial stay of this decision.

The petition for stay should be accompanied by sworn statements by the responsible individuals within the firms in question (manufacturing parties, middlemen, and the larger cattle producers and feed lots) as to the existing stocks of DES. The agency will entertain requests that information regarded as trade secret be kept confidential. See 21 CFR 10.20(j); 514.11(g)(2). The FDA will discount statements that are not sworn. Due to its concern about the possibility of stockpiling, I am announcing now that the FDA will presume that the failure to submit information about the existence of stocks in any major component of the stream of commerce for DES means that large stocks are held by that component.

I should note with respect to the question of the effective date that I reject the argument that, because it has taken the FDA several years to issue a final decision with respect to the DES animal drugs, that decision can be delayed yet a longer time. The delay in the issuance of this decision reflects the importance of the decision and the fact that administrative hearings on complicated issues simply take a long