History of diethylstilbestrol use in cattle[1]

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ABSTRACT: The first demonstration of growth stimulation in cattle with hormone supplementation took place in 1947 by investigators at Purdue University using diethylstilbestrol (DES) in heifers. These studies on DES used a compressed tablet as a subcutaneous implant. Side-effects, such as vulvar swelling, riding, and mammary development, were observed. Scientists at Iowa State College later investigated the efficacy of DES administered orally. Growth stimulation and improved feed utilization were observed in both sheep and cattle, and fewer side-effects were reported with oral use. These studies also demonstrated reduced carcass grade and increased leanness. Orally administered DES for cattle was approved by the U.S. Food and Drug Administration in 1954, and its use in growing-finishing cattle rations was rapidly adopted. Diethylstilbestrol implants were cleared by the Food and Drug Administration for use in cattle in 1957. Later developments defined the optimal dosage and form of orally administered DES. A low incidence of DES residues in the livers of cattle were later found and were associated with misuse. These residues, along with the report of adenocarcinoma in daughters of mothers treated with prescription DES during pregnancy, led the Food and Drug Administration to remove oral DES for cattle from the market in 1972 and implants the following year. The removal of DES from the market led to the development of a number of other growth stimulation products for cattle.

Key Words: Anabolic Steroids, Cattle, Diethylstilbestrol, Growth Promoters, History, Sheep

Introduction

Hormones naturally produced by humans and other animals result in morphological, behavioral, physiological, and biochemical changes. When used for meat production in many parts of the world, bulls are castrated to produce steers in order to reduce aggressiveness, even though this practice reduces growth rate and the efficiency of lean meat production. It is not surprising, then, that animal scientists would be interested in modifying the hormonal status of animals to improve efficiency and product composition. Over the past 42 yr, results of hormonal replacement or hormone supplementation have found widespread application in the production of beef, without any food safety problems for humans or safety problems for cattle. The history of hormonal treatments can be characterized as a series of developments to identify hormone types and to quantify the dosage and form for optimal growth, feed efficiency, carcass quality, and cost of production. This article focuses on the history of the first hormonal modifier that had widespread application and impact in beef production, diethylstilbestrol (**DES**).

Early Research and Application

Enhanced concentrations of thyroid hormones achieved through feeding thyroprotein or iodinated casein were shown to increase milk production in early studies. Estrogenic activity in several plant foods and feeds was found to be responsible for reproductive problems in livestock. Zondek and Marx (1939), in a single cock, demonstrated that the lipemic response at the onset of egg production could be duplicated by injecting estradiol benzoate. In 1943, Lorenz published a note describing the threefold increase in the fat content of the breast and leg muscle 8 wk after implanting DES subcutaneously in cockerels (Lorenz, 1943), a finding that was applied in the commercial production of broilers from 1947 to 1966.

The first experiment that tested the administration of an estrogen, in this case DES, to ruminants for the purpose of growth promotion was conducted at Purdue University by W. E. Dinusson, who was a graduate

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Table 1. Effect of hormone treatments on the growth and fattening of Hereford heifers

Item	Control	Spayed	DES	Testosterone	Thiouracil
No. heifers	5	5	5	5	5
ADG, kg	0.94	0.87[a]	1.05[a]	0.95	0.97
ADF, kg					
Concentrate	4.3	4.8	4.7	4.8	4.5
Roughage	2.9	2.9	3.2	3.0	3.0
Feed/gain	7.7	8.9	7.4	8.3	7.8
Dressing percentage	58.6	59.7	59.8	59.8	58.9
Carcass grade					
Choice, %	80	80	40	80	60
Select, %	20	20	40	20	40
Commercial, %			20		

[a]Difference approached significance ($P < 0.05$) from control.

student of F. N. Andrews[4] and W. M. Beeson. They hypothesized that the growth rate of heifers was increased by estrogen because the growth rate of intact heifers was greater than that of spayed heifers. Diethylstilbestrol was used as the estrogen treatment because DES implants had already been formulated for use in poultry by Wick and Fry, Inc., in Cumberland, IN. Their first experiment, started on February 9, 1947, used 25 Hereford heifers that weighed about 225 kg; the trial lasted for 140 d. Five treatments were studied: control, spayed (spayed before the start of the study), DES (42 mg implanted in the shoulder region), testosterone (50 mg of testosterone propionate injected initially and 32.5 mg injected at 56 d), and thiouracil (4 g·animal^{-1}·d^{-1} in the feed). The diet consisted mainly of corn and cob meal, soybean meal, and mixed clover and timothy hay. The results of this and later studies (Table 1) were first reported November 1948 at the annual meeting of the American Society of Animal Production in Chicago (Dinusson et al., 1948; 1950). A second study, lasting 185 d, was started on December 11, 1947. Three pens of three heifers each, similar to those in the first study, were used on each treatment. The DES implant treatment used was 48 rather than 42 mg, a 50-mg testosterone propionate implant was used rather than oil injections, and a 11 mg/kg BW oral thyroprotein treatment was used rather than thiouracil. Results are shown in Table 2.

The authors reached the following conclusions regarding DES: 1) improved gain and feed conversion; 2) increased length of leg and back, and width of back; 3) increased appetite; 4) carcasses were slightly "hooky" (more mature in appearance); 5) caused vulvar swelling and extended estrus and produced a nymphomaniacal stance, elevated tailheads, and pronounced mammary and teat development. The performance of the spayed heifers was inferior to that of either the control or DES-treated heifers, as had been expected. The authors suggested that "the rate of gain of these three groups was proportional to the amount of estrogen present."

It is interesting to note that these two small studies, using only 14 animals per treatment, predicted quite accurately the utility of DES (estrogen) treatment in feedlot cattle. Diethylstilbestrol generally increased gain by 15%; these studies showed increases of 12 and 17%. Feed conversion improvement was normally about 10%; these studies showed improvements of 4 and 11%. These studies also suggested that leanness increased and carcass grade decreased, both of which were generally experienced with DES. It is also noteworthy that, in the absence of any dose titration studies, the implant dosages selected for use in these studies, 42 and 48 mg, were close to the commonly considered optimal dosage (30 to 36 mg) later used in the feedlot industry.

The side-effects of the DES treatment listed in the conclusion were considered at that time to be very negative and without any immediate apparent solution. These effects, as well as a possible reduction in carcass fatness, undoubtedly delayed the commercial application of this technology.

The first study using DES in finishing lambs also was conducted at Purdue University, by F. N. Andrews in November 1948 (Andrews et al., 1949). The authors concluded that DES implants improved gain and feed conversion and reduced carcass grade. Because of its carcass effects, DES appeared to have stimulated "true growth" in these lambs. The only side-effect reported was the loss of one lamb in a 12-mg group due to prolapsed rectum. In contrast to the cattle studies, the DES implant doses (12 and 24 mg) used in this study were considerably higher than those ultimately used in practice (3 mg).

Oral Administration of DES

Diethylstilbestrol was synthesized initially as an orally effective estrogen for use in human medicine (Dodds et al., 1938) and was used to prevent miscarriage. The first report of the effects of oral administration of DES in ruminants was by W. H. Hale at the

[4]A biographical sketch on Andrews is available at this Web site.

Table 2. Effect of hormone treatments on the growth and fattening of heifers

Item	Control	Spayed	DES	Testosterone	Thyroprotein
No. heifers	9	9	9	9	9
ADG, kg	0.78	0.70[a]	0.91[a]	0.78	0.72
ADF, kg					
Concentrate	5.4	5.1	5.7	5.3	5.4
Roughage	3.3	3.2	3.3	3.3	3.3
Feed/gain	11.1	11.9	9.9	11.0	12.0
Dressing percentage	60.8	59.8	60.6	60.1	60.4
Carcass grade					
Choice, %				11	
Select, %	78	78	56	56	56
Low select, %	11	22	44	22	44
Commercial, %	11			11	

[a]Difference was significant ($P < 0.05$) from control.

1953 American Society of Animal Production meeting, in Chicago, IL (Hale et al., 1953). Hale and his graduate student C. D. Story at Iowa State College fed levels of DES that they felt were comparable in estrogenic activity to the levels found in certain legumes purported to increase growth rate. They fed DES at 3.3 to 26.5 mcg/kg of diet. In two studies, the lower levels of DES (3.3 to 6.6 mcg/kg) improved both gain and feed conversion, whereas the higher levels had no effect. A third study found no benefit from orally administered DES. The responses in the first two studies are unexplainable, because the effective oral dosages were found later to be from 660 to 1,320 mcg/kg of diet (Hale et al., 1955). Even though these initial experiments on the oral administration of DES did not show a consistent response, they led to other critical studies at Iowa State College.

Hale and W. Burroughs, a coauthor on the Hale papers, discussed the idea of feeding DES to cattle. Although DES was not very effective orally in chickens, Hale had seen a research note in a British pharmaceutical journal (source unknown) indicating that DES was rapidly detoxified in chickens but not in cattle (W. H. Hale, personal communication). Hale and Burroughs conducted a small experiment at the Beech Avenue cattle facility at Iowa State using individually fed cattle that indicated that there may be a response to a "high level" of DES (unpublished results).

In the spring and summer of 1953 at the Iowa Southwestern Experimental Farm, Burroughs conducted an experiment that indicated that "cattle gains could be increased substantially and that feed costs could be reduced materially by placing 5 mg or more of DES in the daily supplemental feed fed to each steer" (Burroughs et al., 1954b). In subsequent cattle feeding studies, he fed levels of 2.75 to 20 mg·animal^{-1}·d^{-1} to yearling steers fed corn-corn silage or corn-corn cob fattening diets for periods of 46 to 120 d (Burroughs et al., 1954a, 1955; Culbertson et al., 1954). Results of three of these studies are shown in Table 3. Burroughs concluded that DES increased gains by up to 35% and reduced feed cost by up to 20%. He also reported that in these studies no reduction in fatness or meat quality was observed. None of the undesirable side-effects previously reported with DES implants were observed. He noted that cattle feeders would not find DES implantation to be practical for the following reasons. 1) A potential human health hazard exists if substantial pellet residues remain in tissues at slaughter. 2) Diethylstilbestrol implantation appears to adversely influence carcass quality. 3) Implanted animals may exhibit undue restlessness or abnormal sexual behavior. 4) Some animals may exhibit toxicity symptoms (such as uterine and rectal prolapse and difficulty in urination) from DES implantation. In contrast, he suggested that *feeding* DES was practical because of the ease of administration, no undesirable side-effects, and the potential to withdraw the compound and because feeding allows the accurate administration of a constant dosage. The biological effects of DES in cattle and lambs has been reviewed (Preston, 1975).

Special Iowa State Feeders Day

On February 18, 1954, a special Cattle Feeders Day was held at Iowa State University to announce the discovery of the growth promotion by oral DES in cattle. Previous publicity about a new discovery resulted in a huge and unexpected crowd (over 1,000). To accommodate the crowd, the morning and afternoon programs were presented simultaneously. There were insufficient copies of the research report; one of us (R. L. Preston) overheard some cattle feeders saying that without a report, they would not be able to show their wives where they had been that day.

Iowa State Patents Oral DES

Purdue University made no attempt to obtain patent protection for the use of DES implants in cattle and sheep (Andrews, 1995). The Purdue administration at that time felt that commercialization of any new technology was beyond the academic role of the university (T. W. Perry, personal communication). However, Iowa State College and W. Burroughs filed for a U.S. patent

Table 3. Effects of diethylstilbestrol in the diets of fattening steers[a]

	Amount DES·steer^{-1}·d^{-1}			
Item	0	2.5 mg	5 mg	10 mg
Exp. 1; 46 d				
ADG, kg	0.96		1.29[b]	1.13
Feed/gain	11.4		9.3	10.6
Exp. 2; 84 d				
ADG, kg	1.13	1.23	1.43[b]	1.55[b]
Feed/gain	11.6	10.8	10.0	9.1
Exp. 3; 84 d				
ADG, kg	1.14		1.43[b]	
Feed/gain	9.1		8.3	

[a]Eight steers per treatment.
[b]Significantly different ($P < 0.05$) from 0 control.

on the oral administration of DES to cattle on June 3, 1953; it was granted in May of 1956. Eighty-five percent of the royalties from the patent accrued to the Iowa State College Research Foundation. The patent was based on many of the advantages of feeding DES over implanting suggested in Burroughs's publication in *Science* (Burroughs et al., 1954a). At that time, J. F. Downing had the responsibility for finding and developing new animal products for the recently formed Agricultural Products Division of Eli Lilly and Co., Inc. The president of Specified, Inc. (an agriculture/pharmaceutical company) in Indianapolis, IN, Downing's previous employer, was returning to Indianapolis after attending a Cattle Feeders Day program at the University of Minnesota. Seated in front of him on the plane were two people discussing the results of the DES studies at Iowa State. As soon as the plane landed, the president of Specified, Inc., called Downing and passed on what he had heard. Downing immediately contacted the Lilly patent counsel, called Burroughs, and arranged a meeting at Iowa State the following day. Iowa State had made contact earlier with a potential DES manufacturer for development of the product but had received a noncommittal response. Lilly, also a manufacturer of DES, came to the meeting ready to make a commitment to further research and development. Lilly also possessed some manufacturing technology that was critical to the safe handling of the drug. As a result of this meeting, and after the president of Iowa State University, J. H. Hilton, met confidentially with interested parties in agriculture, Iowa State College granted an exclusive 5-yr license under the patent to Lilly on July 29, 1954 (Willham, 1996).

Lilly worked with Iowa State College in developing the data needed for the approval of DES by the Food and Drug Administration (**FDA**). The tissue residue was measured using an immature mouse uterine weight, parallel line bioassay with a sensitivity of 2 to 3 ppb (Preston et al., 1956). The registration package was submitted to the FDA, and DES was approved to be fed to beef cattle at a level of 10 mg·animal^{-1}·d^{-1} on November 5, 1954. Clearance came only 1 yr after the report of the results from the first DES cattle feeding studies. Within 4 wk after FDA approval, the DES premix Stilbosol was available to feed manufacturers. Stilbosol was the product that provided the foundation for the development of the animal product business of ELANCO Animal Health.

A quote from A. Marcus (Marcus, 1994) characterizes the university-industry partnership that was at work at that time: "Indeed, the case of DES seemed to be a model of the application of the partnership idea. A college scientist uncovered a new technique, pharmaceutical scientists produced the drug, feed-manufacturing scientists compounded the material as a premix, federal scientists approved its use, agricultural college scientists publicized it by demonstrating its utility, and farmers made use of it. That type of expert-based interaction had been the model for 'progress' since the 1920s. With respect to stilbestrol, little in the mid-1950s seemed to undercut faith in that model." Today, this partnership still exists except that pharmaceutical scientists have taken the lead in developing new drugs and combinations.

DES Implant Development

DES implants for poultry were formulated by Bill Wick and Henry Fry, formulation chemists for Eli Lilly and Co., Inc. This development work was a "moonlight" project carried out in their personal laboratory, a converted garage in Cumberland, IN. They approached George Varnes, president of the newly formed Lilly Industrial and Agriculture Products Division, to determine whether Lilly had an interest in developing DES implants for cattle. Varnes indicated that he was not optimistic about the commercial possibilities for the use of growth-promoting implants in beef cattle and declined the offer (T. M. Means, personal communication). Wick and Fry then cooperated with Chas. Pfizer, Inc., Terre Haute, IN, in the development of DES implants for use in cattle. Pfizer obtained FDA approval for DES implants for cattle in 1957.

Table 4. Effect of oral and implanted diethylstilbestrol on the feedlot performance of yearling steers

Item	Control	10 mg oral	10 mg oral + 15 mg implant
No. steers	35	34	36
ADG, kg	1.21	1.32	1.42
ADF, kg	12.1	12.2	12.2
Feed/gain	10.1	9.2	8.7
Dressing percentage	59.2	59.2	59.2
Carcass grade[a]	6.9	7.1	6.8

[a]6 = low Choice, 7 = avg. Choice.

Table 5. Effect of two daily doses of orally administered diethylstilbestrol on feedlot performance of steers

Item	10 mg	20 mg
No. steers	63	62
ADG, kg	1.01	1.07
ADF, kg	10.4	10.5
Feed/gain	10.25	9.86
Dressing percentage	59.0	59.2
Carcass grade[a]	5.50	5.25

[a]6 = low Choice, 7 = avg. Choice.

Oral and Implanted DES Used Together

With two commercial product forms available and no specific regulation preventing their simultaneous use, it was inevitable that innovators would try simultaneous use of implant and oral DES in an attempt to produce greater gain and efficiency. Experiments showed a larger total response to DES, particularly in heavier cattle. The results of one of these experiments are shown in Table 4. This Iowa State study used 345-kg yearling steers fed a typical corn, hay, and supplement diet for 126 d (Burroughs et al., 1963). Greater responses were observed with the dual oral and implant DES treatment. Gain was increased 9% by the 10-mg oral treatment and 17% by the dual treatment, but carcass grade tended to be reduced by the combination treatment. The dual usage of oral and implanted DES was widely used in feedlots even though FDA ruled that dual usage violated regulations, but they could enforce this ruling only by finding residues in slaughtered cattle by the approved method, the mouse uterine weight assay.

Oral 5 to 20 mg of DES Approved for Cattle

At the time of the original DES clearance for cattle, there were data suggesting that levels of DES higher than 10 mg would produce greater response. However, at that time Burroughs and his coworkers (Culbertson et al., 1954) felt that the 10 mg dosage was close to being optimum and was the best compromise. At that early time there may have been concern about potential side-effects with widespread use in the field. However, the dual usage clearly showed that 10 mg was not the optimal dose and that higher dosages were manageable. Data were developed to support the clearance of feeding a variable dosage of DES (5 to 20 mg/d); this was approved in 1970. One of the comparisons of the efficacy of 10 and 20 mg is shown in Table 5 (Raun and McAskill, 1965). This study used yearling steers averaging about 385 kg and fed a complete mixed finishing diet for 127 d. The higher dosage of DES increased rate of gain about 6% and reduced feed required per unit of gain about 4%. Carcass grade appeared to be reduced.

Low Bioassay DES Found To Be Less Effective

It became a common practice to assay feed and premixes for DES using a chemical assay. It was observed that some feeds and premixes were at or near theoretical DES levels by chemical assay but, when assayed biologically using the mouse uterine weight assay, in some cases were only about 50% of theory (Raun et al., 1970; Hutcheson and Preston, 1971). It was found that these low bioassay DES premixes contained up to 24% of the *cis*-isomer. Purified or enriched preparations of *cis*- and *trans*-isomers of DES were prepared, and the efficacies of these two forms were compared in a number of studies (Raun et al., 1970; Preston et al., 1971). The results of one of the cattle efficacy studies are shown in Table 6. Little if any response was noted with the cis-DES treatment, whereas the expected response were observed with the purified trans-DES. Early in 1970, a stabilized trans-DES premix was introduced into the market. By this time, multiple companies were suppliers of DES, operating under a sublicense to the Iowa State/Lilly patent agreement. This premix was promoted by ELANCO as "High Trans Stilbosol," and it had an immediate and dramatic effect on market share. This product designation had to be removed because the FDA ruled that an efficacy claim was being made without submission of data. Even though the "High Trans" product identification could not be used, the stabilized premix continued to be used as Stilbosol.

The Rise and Fall Of DES in Cattle Feeding

By the end of 1955, 1 yr after the approval of oral DES, an estimated six million cattle (~50%) were being

Table 6. Effect of 10 mg of orally administered *cis*- and *trans*-isomers of diethylstilbestrol on performance of feedlot steers

Item	Control	*cis*- (89%)	*trans*- (100%)
No. steers	20	20	19
ADG, kg	1.10	1.11	1.30[a]
ADF, kg	7.7	7.6	8.1
Feed/gain	7.04	6.85	6.29

[a]Greater than cis-diethylstilbestrol ($P < 0.05$).

fed DES. Eventually, 80 to 95% of the fed cattle received DES in some form. Early on, however, there were industry concerns and misconceptions about the effects of DES. Physiological (high tailheads and teat development) and behavioral (estruslike) "observations" were mentioned, mostly because of early experimental observations. Carcass grade and dressing percentage reduction were used by packer buyers to reduce the price paid for cattle, something that still plagues users of implants today (Preston, 1993). Carcasses from cattle given DES were said to be soft and cut "dark." It was claimed that water retention was responsible for the growth response to DES, something later proven false using radioactive water (Preston, 1969). These concerns culminated in a special "packer" meeting at Iowa State on a Saturday (April 16, 1955) when data on carcass effects were presented; this diminished the rumors somewhat at that time. Cornbelt feeders accustomed to feeding small- to medium-framed cattle on high-corn silage diets to a certain final BW did not realize that higher energy diets and heavier final weights were required to achieve the same carcass grade, because DES increased mature BW (Preston, 1978).

The popular and scientific press also misrepresented the safety of beef produced using this new technology. The *Police Gazette* ran the cover headline "Beef Will Make You Sterile." Nicholas Wade published a "science news" article in *Science* (Wade, 1972), in which he described DES as "a chemical of bizarre and far-reaching properties, chief of which is that it is a spectacularly dangerous carcinogen" and accused the FDA of political manipulation in an election year. Tom Jukes (Jukes, 1976) and others repeatedly pointed out the infinitesimal risk of cancer from eating beef produced using DES. Yet, the FDA was under considerable congressional pressure to enforce the Delaney amendment prohibiting the use of any carcinogen if there was a residue in food, the so-called zero residue amendment. One person advocated that "Congress needed to enact legislation outlawing all substances that caused cancer in any species, even if no evidence existed that these materials could produce cancer in man" (Marcus, 1994). The FDA maintained the position that residues were not found in beef based on the mouse uterine weight assay that was sensitive to 2 to 3 ppb. During the 1960s, it was found that about 0.5% of the livers, the primary organ of DES excretion, but not the meat of commercial cattle at postmortem inspection had detectable residues. In the early 1970s, however, this incidence rose to 2 to 2.5%, probably because of dual usage, higher oral doses, and most importantly, a lack of adherence to the required withdrawal periods. The FDA prosecuted cattle feeders who did not use DES correctly. The USDA studies using ^{14}C-labeled DES (Aschbacher and Thacker, 1972) detected presumed residues (<2 to 3 ppb) based on total radioactivity. Because the carcinogenic level of DES in cancer-prone laboratory animals was equivocal (Cole et al., 1975), the FDA maintained that the carcinogenicity of DES in humans had not been demonstrated. However, Herbst et al. (1971) reported adenocarcinoma in daughters of mothers that had taken massive doses of prescribed (mistakenly as it turned out) DES (up to 125 mg daily) during the first trimester of pregnancy for the prevention of threatened miscarriage. The FDA then had no option except to ban the use of DES in cattle production, even though Herbst et al. (1971) later pointed out that this disease was extremely rare even among the DES-exposed group.

Thus the time-line for the rise and fall of DES is as follows.

1954 FDA approves oral DES feeding.
1957 FDA approves DES implants.
1959–1975 USDA isotope studies show DES residues of < 2 to 3 ppb.
1972 FDA bans oral DES; 120 d withdrawal for DES implants.
1973 FDA bans DES implants. FDA prosecutes cattle feeders with "DES-contaminated" cattle.
1974 U.S. Court of Appeals overturns ban; FDA failed to hold proper hearings.
1977 FDA holds DES hearings.
1979 FDA bans all use of DES in cattle production.

Epilogue and Chronology of Anabolic Agents

The use of DES in cattle and sheep became the victim of zealous attempts to protect the public from all risk. The evidence indicates that the use of DES in cattle and sheep was not treated objectively by politicians and the press who put unbelievable pressure on the FDA. As Marcus (1994) said, "no one could prove that DES beef had harmed a single member of the populace. Conversely, no one could prove that it had not." It is our opinion that if DES had not been banned it would still rank as one of the most effective cattle growth promotants and that human safety would have never been compromised with proper use.

Chronology of Cattle Anabolic Agents in the United States

1954 Oral DES approved for cattle.
1955 DES implants approved for cattle.
1956 Estradiol benzoate/progesterone implants approved for steers.
1958 Estradiol benzoate/testosterone propionate implants approved for heifers.
1968 Oral melengesterol acetate approved for heifers.
1969 Zeranol implants (36 mg) approved for cattle.
1982 Silastic estradiol implant approved for cattle.
1984 Estradiol benzoate/progesterone implants approved for calves.

1987 Trenbolone acetate implants approved for cattle.
1991 Estradiol/trenbolone acetate implants approved for steers.
1993 Bovine somatotropin approved for lactating dairy cows.
1994 Estradiol/trenbolone acetate implants approved for heifers.
1995 72-mg zeranol implants approved for cattle.
1996 Estradiol/trenbolone acetate implants approved for stocker cattle.

Implications

Feeding diethylstilbestrol offered dosage and withdrawal control not available in implant products. However, the removal of diethylstilbestrol from the marketplace forced the development of a number of alternative products. These products came to the market only after significant expenditures of research time, money, and regulatory agency effort. If diethylstilbestrol had not been removed, these same resources could have been directed toward the discovery, development, and approval of other technologies for the cattle industry. It is disappointing that we still do not have a clear explanation for the mode of action of estrogen growth promotants in cattle and sheep.

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