GROWTH STIMULANTS: COMPOUNDS, CONCENTRATIONS, COMBINATIONS AND REGULATIONS

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ABSTRACT

Over the past fifteen years, the number and type of growth promotant implants available for improvement of beef productivity has increased dramatically. Currently, ten New Animal Drug Approvals (NADA's) cover products marketed under nineteen different tradenames. All growth promotant implants are regulated by the Food and Drug Administration (FDA). The implants can be classified as either single ingredient or combination ingredient products that contain estrogens, androgens or progestins. The best source of information on products can be found on the product label or insert or from Freedom of Information documents available through Freedom of Information Services, Washington, DC.

INTRODUCTION

Growth promotant implants have been available since the mid-1950's for improving average daily gain and feed conversion in beef cattle. Implants are approved and regulated by the Food and Drug Administration. Information on products is best obtained from the product label or insert; however, for more complete information on a product, Freedom of Information documents can be obtained from:

Food and Drug Administration
Freedom of Information Staff
HFI-35
5600 Fisher Lane
Rockville, MD 20857

All implants currently on the market contain active ingredients which can be classified as estrogens, androgens or progestins. Table 1 identifies the different active compounds found in implants; melengestrol acetate is available only as a feed additive.

Utilizing these active ingredients either alone or in different combinations and at various concentrations has resulted in thirteen different products marketed under nineteen tradenames. These different products can be divided into single ingredient or combination ingredient products. Single ingredient products contain either estradiol 17 B, zeranol or trenbolone acetate at various concentrations (Table 2).

Table 1. Hormonal Growth Promotant Compounds

Estrogens
- Estradiol 17B (E2)
- Estradiol benzoate (EB ⇒ 71% E2)
- Zeranol (Z)

Androgens
- Testosterone propionate (TP)
- Trenbolone acetate (TBA)

Progesterones
- Progesterone (P)
- Melengestrol acetate (MGA)

The combination products (Table 3 and 4) contain estradiol benzoate/ progesterone, estradiol benzoate/ testosterone, estradiol benzoate/ trenbolone acetate or estradiol/trenbolone acetate with various concentrations of each of these active ingredients. These concentrations and combinations have been utilized for the approval of the products in steers and heifers during different stages of production, i.e., calf, stocker and feedlot.

Implants are manufactured as compressed pellets; pellets per dose ranges from three to ten based on the product. Exceptions are the estradiol products Compudose and Encore which utilize a single silastic rubber implant as the support matrix for the active ingredient. This carrier, being non-absorbable, remains with the animal indefinitely.

When comparing products for estrogen content, it is important to convert the compound its active ingredient, estradiol 17 B. For example, in the case of Synovex Plus, the 28 mg of estradiol benzoate equals 20 mg of estradiol 17 B because estradiol benzoate contains only 71.4% estradiol 17B.

The "Indication of Use" reflects where a product is approved for use and the sex for which it is approved. As indicated earlier, the segment of use can be feedlot, pasture and(or) suckling calf.

Table 2. Concentrations and Trade Names of Single Ingredient Implants

Ingredient	Concentration (mg)	Trade Name
Estradiol	25.7	Compudose®
	43.9	Encore®
Zeranol	36.0	Ralgro®
	72.0	Ralgro Magnum®
Trenbolone Acetate	140	finaplix® - S
	200	finaplix® - H

Table 3. Concentrations and Trade Names of Combination Ingredient Implants

Ingredient	Concentration (mg)	Trade Name
Estradiol benzoate	20 (14 E2)	Synovex® S
Progesterone	200	Implus® S
		Component® E-S
Estradiol benzoate	10 (7 E2)	Synovex® C
Progesterone	100	Implus® C
		Component® E-C
Estradiol benzoate	20 (14 E2)	Synovex® H
Testosterone propionate	200	Implus® H
		Component® E-H
Estradiol	24	revalor® S
Trenbolone acetate	120	
Estradiol	14	revalor® H
Trenbolone acetate	140	
Estradiol	8	revalor® G
Trenbolone acetate	40	
Estradiol benzoate	28 (20 E2)	Synovex® Plus
Trenbolone acetate	200	

Table 4. Indication of Use for Feedlot Cattle

		Improved ADG		Improved FE	
		Steer	Heifer	Steer	Heifer
Estradiol	25.7+	X	X	X	X
	43.9++	X	X	X	X
Zeranol	36	X	X	X	X
	72	X			
TBA	140*			X	
	200**		X		X

* Reimplant once after 63 days for continued effectiveness.
** Use only the last 63 days prior to slaughter.
\+ Effective daily dose for at least 200 days.
++ Effective daily dose for at least 400 days.

Table 5. Indication of Use of Combination Implants for Feedlot Cattle

		Improved ADG		Improved FE	
		Steer	Heifer	Steer	Heifer
EB/P	(20/200)*	X		X	
EB/T	(20/200)		X		X
E2/TBA	(24/120)	X		X	
	(14/140)		X		X
EB/TBA	(28/200)			X	

* Synovex S - Reimplant after 70 days for additional improvement in ADG.

For the feedlot phase of cattle production, six single ingredient products are approved (Table 4) and five combination products are approved (Table 5). The claims for these products reflect whether they received approval to improve average daily gain and feed conversion in steers or heifers. The single ingredient estradiol products also carry a time claim for an effective life span of 200 and 400 days for the 25.7 and 43.9 mg products, respectively.

Some of the products, such as the zeranol 72 mg product (Ralgro Magnum) and the TBA 140 mg product (finaplix S) carry claims for only gain or feed conversion. This does not necessarily mean that the product is not effective for the other claim, only that an additional claim was not supported by the data that was submitted to the FDA. In general, additional information is provided to the public by the marketer after approval by the FDA for better assessment of the product under different feeding conditions. Currently all combination products have been approved on a gender specific basis. The Synovex S and finaplix S implants also carry specific reimplantation claims for additional or continued improvement in gain or feed conversion, respectively.

In the pasture phase of production, there currently are three single ingredient products approved and three combination products approved (Table 6). All products in this phase of production have approval for average daily gain.

The 25.7 and 43.9 mg estradiol products only have approval in steers. The latest approval on pasture was received in 1995 for a reduced dosage of E2/TBA (8/40).

In the calf phase of production there are three single ingredient and one combination ingredient products approved (Table 7). The estradiol products again only have steer approval while the zeranol and E2/progesterone products have both steer and heifer approval. In addition to improved average daily gain, Ralgro and Synovex C have approval for use in heifers that may later be used for replacement purposes. Heifers that are to be kept for replacements should be implanted no sooner than 30 or 45 days of age for Ralgro and Synovex C respectively.

The final area for consideration is warnings and cautions associated with the use of the implants. These areas concern possible side effects, implantation site and situations where implants should not be used. Implantation site for all implants is in the ear. Any other implant site is in violation of Federal law. Growth promotant implants should not be utilized for dairy cattle and bull calves intended for reproductive purposes. Other considerations for use of implants are shown in Table 8. Labels should be read completely for information on these areas.

Table 6. Pasture Implants

		Improved ADG	
		Steer	Heifer
Estradiol	25.7	X	
	43.9	X	
Zeranol	36	X	X
EB/P	(20/200)	X	
EB/T	(20/200)		X
E2/TBA	(8/40)	X	X

Table 7. Implants for Suckling Calves

		Improved ADG		
		Steers	Heifers	Replacement Heifers
Estradiol	25.7	X		
	43.9	X		
Zeranol	36	X	X	30 day
EB/P	(10/100)	X	X	Synovex C 45 days

Table 8. Major Considerations

Item	
Implant Location (All)	Implant in the ear only. Any other location is a violation of Federal law.
Implant Withdrawal (All)	No withdrawal prior to slaughter.
Possibly decreased marbling scores	revalor S, revalor H, Synovex Plus Synovex S reimplant
Bulling, vaginal and rectal prolapse, udder development, signs of estrus	E2, EB/P E2, EB/T, Z
Use in breeding herd replacements and dairy animals	Do not use (except Synovex C and Ralgro in beef replacement calves).
Storage (room temperature)	E2, Z, EB/P, EB/T, EB/TBA
Storage (refrigerated)	E2/TBA, TBA

Holders of the implant NADA and marketers of the implants have changed dramatically over the past 12 months due to consolidation of companies. Current holders, manufacturers and marketers of growth promotant implants are listed in Table 9. As trends for consolidation may continue, this area should be updated routinely.

Growth promotant implants are approved in a number of countries including: Australia, New Zealand, Canada, Mexico, South Africa, Columbia, Chile, Japan and Argentina. Readers should check with the NADA holder to determine the international approval status of specific products of interest.

Table 9. Holders of NADA, Manufacturers and Marketers

Product	NADA Holder	Manufacturer	Marketer
Synovex	Ft. Dodge Animal Health	Syntex, Inc. Palo Alto, CA	Ft. Dodge Animal Health
Ralgro	Mallinckrodt	Mallinckrodt Terre Haute, IN	Mallinckrodt
Compudose	Elanco Animal Health	Elanco Animal Health, Mexico	VetLife, Inc.
Finaplix Revalor	Roussel UCLAF	Roussel UCLAF Hoechst	Hoechst
Implus Component	Ivy Laboratories	Ivy Laboratories Overland Park, KS	Upjohn VetLife, Inc.

QUESTIONS & ANSWERS

Q: Why does Synovex not have a claim for improving feed efficiency in cattle?

A: Information submitted for clearance probably was inadequate for this claim. Others from the audience might address this question further.

Q: Why do the labels not specifically state "zero withdrawal required"?

A: You would think that the FDA would want to include that information on the label. But that hasn't been the case so they haven't been put on there. Also, in the early years, some products had withdrawal times. For example, I think Ralgro had a withdrawal period of days following implanting whereas other implants had zero withdrawals and maybe the FDA thought that such a statement might affect the concept of relative safety of two different products.