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Hormonal Growth Promotant (HGP) use in the Australian Beef Industry

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Abstract

This review compiles and interprets scientific studies relevant to the use of hormonal growth promotants (HGPs) by Australian beef producers. It details the chemical formulations of the range of products registered for use in Australia and their modes of action in promoting growth. Particular attention is devoted to the magnitudes and durations of the growth responses under pastoral and feedlot conditions in Australia. The effects of single and repeated implantation on body composition and beef eating quality are described. The scientific principles that underpin implantation strategies designed to prepare cattle for target market specifications are discussed. Concluding sections deal with the effects of HGP treatment on the fertility of breeding females and on bulls, as well as the side-effects and animal behaviour.

Contents

Introduction

Hormonal growth promotants (HGPs) have been used in the Australian beef industry for the last 30 years. There is sufficient scientific evidence to establish that growth rate is increased by 10-30%, feed conversion efficiency by 5-15% and carcass leanness by 5-8% [(1)]. Their use in Australia has been steadily increasing over the last decade. Six and a half million doses were sold in the year ending March 2007; up from 5.8 million in the corresponding period to March 2006 [(2)]. This 12 % increase in sales wa1s against a decrease in the Australian herd size of 1.2 % in the corresponding period.

Meat and Livestock Australia (MLA) statistics recorded that in the 2007-08 year Australia produced 2.15 million tonnes of beef (carcass) from its 28.04 million head of cattle. The slaughter numbers for 2007 were 8.05 million head. A reasonable estimate is that about 50% of implanted cattle receive two implants during their grow-out and finishing [(3)]. This equates to, on average, 1.5 implants during the life of HGP treated cattle. Assuming that implantation occurs in each of the final two years before slaughter, it can be calculated that 4.1 million of the 8.05 million cattle slaughtered were implanted. Further, if it is assumed that growth rate and carcass weight of the implanted cattle are increased by an average of 15 %, it follows that 0.16 million tonnes of the national beef production, or 7-8 %, was attributable to use of HGPs. On these figures, the national herd would have to increase to 30.28 million to produce the same tonnage of HGP free beef. Such a national herd population is not unprecedented as MLA statistics record that it was over 30 million in the mid 1970s, peaking at 33.4 million in 1976.

An economic evaluation of HGP use in Australia, conducted in conjunction with this scientific review, estimated that HGP usage contributed an additional $210 million to the Australian beef industry in 2006-07 [(4)]. The $80 million additional value to the feedlot sector was principally associated with lower feed costs per unit of liveweight gain. In some cases, the boost in growth rates from HGP use allowed cattle to meet the liveweight and age specifications for higher priced markets. The $130 million of additional value to the grass-fed sector resulted principally from earlier turnoff and the associated increase in numbers of cattle marketed.

HGPs are used extensively in feedlots and in the grass-fed industry of northern Australia. It is estimated that at least 80 % of cattle are implanted at feedlot induction [(5)]. In the northern Australian grass-fed industry, HGPs are used as a management tool in preparing steers for higher value markets. The highly seasonal nature of pasture quality in this region means that cattle often must meet market specifications for age and weight before pasture senesces, causing a rapid decrease in the rate of liveweight gain. This is illustrated diagrammatically in Figure 1. The additional liveweight gain from an HGP program can mean the difference between steers meeting the specifications for a higher value market or being consigned to lower value markets such as the USA grinding beef trade.

The annual audits of HGP sales by Animal Health Alliances Australia show that since the European Union (EU) ban on HGPs in 1988, the usage in southern Australia has decreased markedly. Although the export quota to the EU is small, currently 7,150 tonnes of beef per year, producers do not wish to limit their market access options. In addition, the nutritional environment is usually not as severe, or as fluctuating, as in northern Australia. Cattle can generally meet the age and weight specifications for premium markets without the added growth boost from a HGP. The Tasmanian Government has legislated that HGPs not be used in the Tasmanian beef industry, presumably to create a niche market for Tasmanian beef.

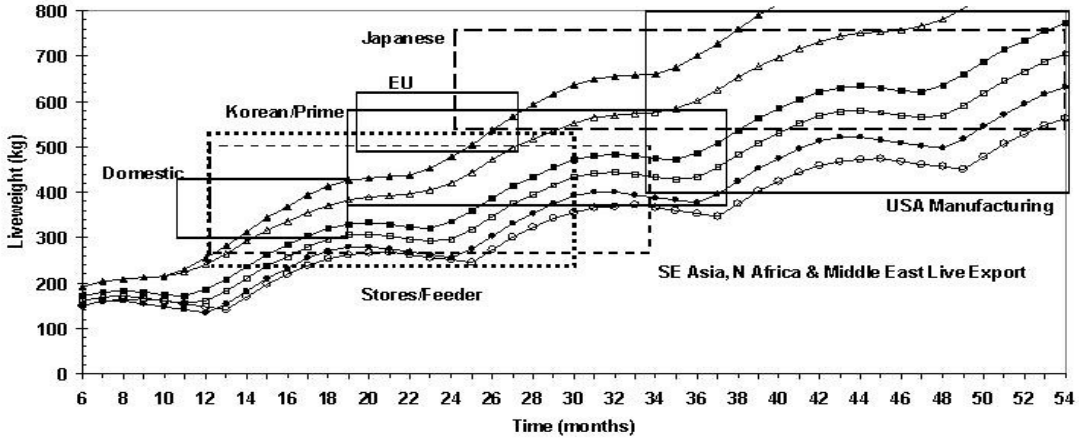

Figure 1[1]. Seasonal growth curves for various annual liveweight gains (100 (○), 120 (●) 135 (□), 150 (■), 180 (∆) and 220 (▲) kg/year) for grazing cattle in northern Australia in relation to live cattle and meatworks market specifications. (*Figure supplied by Dr Greg Bortolussi and reproduced with permission of Dr Bortolussi and Dr Chris Anderson, Managing Editor, Australian Journal of Experimental Agriculture.*)

The Australian beef industry is increasing in complexity and sophistication. There is a bewildering number of pure breeds, stable crossbreeds, composites and rotational breeding programs, all producing slaughter generation off-spring with different rates of maturity and different carcass compositions at any given weight. In addition to the domestic market which takes about 33 % of total production, there are numerous export markets with different requirements for carcass composition. Some demand leanness, some require fatness, while others expect fat in one anatomical region of the carcass and preferably not in others. Similarly the types of HGP implants are complex. All promote liveweight gain, but the effect on partitioning of nutrients between carcass protein and fat varies. Some implant formulations have a longer functional life than others and some individual hormones may have a greater influence on meat eating quality than others. To meet consistently the specifications for a target market, producers need to manage the genetic and non-genetic factors that influence product quantity and quality. HGPs are commonly used as a component of the management package. Sometimes their use may not be beneficial. This is likely to occur in production systems in which late maturing genotypes are used to produce beef for markets which require a substantial degree of fatness at light carcass weights. Other markets discount HGP treated beef on the grounds of reduced eating quality. In both cases, payment for the additional carcass weight might not compensate for the reduced price per kilogram of beef.

The focus of this review is use of HGPs under Australian conditions, particularly in the northern grass-fed industry and in feedlots where they are used extensively. Citing Australian scientific reports and Australian data has been a priority. Some of these data have not been through a scientific peer review process, which does not imply that the conclusions are not correct, but does mean that the conclusions may not be viewed with the same degree of confidence as those subject to peer review prior to publication. The form of citation in the bibliography gives an indication of scientific status of the reference information. International scientific literature has been used to

[1] Bortolussi G, McIvor JG, Hodgkinson JJ, Coffey SG, Holmes CR (2005). The northern Australian beef industry, a snapshot. 3. Annual liveweight gains from pasture based systems. *Australian Journal of Experimental Agriculture*. **45**, 1093-1108.

describe the more theoretical aspects of HGP use as this information is not generally available in the scientific literature generated by Australian scientists.

Formulations of products registered for use in Australia

Chemical compounds used in HGP implants in Australia are:

- oestrogen (oestradiol 17-β, oestradiol benzoate).
- zeranol, a non-steroidal compound isolated originally from fungus infected maize, belonging to a class of compounds known as β-resorcylic lactones.
- progesterone.
- testosterone (testosterone propionate).
- trenbolone acetate (a synthetic androgen).

Oestrogenic compounds (of which zeranol is classed as one) are the major class of growth promoting hormones and, with one exception, are a component of all implants registered for use in Australia. The exception contains only trenbolone acetate and is intended for use in animals where there is endogenous oestrogen production or in animals which have been already implanted with an oestrogen. Oestrogenic activity is an apparent requirement for growth promotion as other oestrogen-like compounds, without oestrogenic activity, do not promote growth [6,7,8].

Progesterone is included in one class of implant in combination with oestradiol benzoate. There is no clear evidence that progesterone promotes growth. However it does reduce oestrogen induced teat growth in cattle [9] and may be included for this reason.

The growth promoting effect of the androgens (testosterone and trenbolone acetate) in the absence of a companion oestrogen are not as reliable as that of oestrogens. At dose rates in the physiological range that can be delivered by implants, testosterone propionate does not promote growth at growth rates under about 0.8 kg/d [10,11,12]. Likewise trenbolone acetate was found not to promote growth of steers at pasture, gaining less than 0.8 kg/d [13]. At growth rates greater than 1.0 kg/d, steers treated with testosterone propionate [11,12] do grow faster than untreated steers.
Trenbolone acetate is a synthetic androgen with 3-5 times the androgenic activity and 8-10 times the anabolic activity of testosterone [14]. It promotes growth alone at high growth rates [15] and in combination with an oestrogen at all growth rates.

The formulations of products currently used in Australia are listed in Table 1. Also listed are the types of cattle for which the products are registered, the types of binding matrix of the compressed pellet implants together with the withholding periods. Frequently similar formulations of hormones are marketed under different product names.

There are essentially two delivery systems for the hormones. All products except Compudose 100, 200 and 400 in which oestradiol-17β is impregnated into the silicone rubber (Figure 2) are compressed pellet implants. They are made like pharmaceutical tablets by compressing the active ingredients with a carrier matrix which is usually based on lactose, cholesterol or polyethylene glycol (PEG). The carrier is about 15 % of the compressed pellet implant by weight and the dose rate of the hormones is controlled by the number of pellets in the implant. For example, Revalor G (60 mg trenbolone acetate plus 12 mg oestradiol-17β) has 3 pellets and Revalor S (140 mg trenbolone acetate plus 28 mg oestradiol-17β) has 7.

Table 1. Formulation of hormonal growth promotants registered for use in Australia

Product name	Hormone formulation (per implant)	Implant Type	Carrier Matrix	Label statement for use	Withholding period for beef production
Compudose 100	21.1 mg oestradiol-17β	Silicone rubber	Silicone rubber	Increased weight gain in pastoral steers including suckling steers and in spayed heifers and vealer calves. Improved feed efficiency and increased weight gain in lot-fed steers and spayed heifers	Nil
Compudose 200	25.7 mg oestradiol-17β	Silicone rubber	Silicone rubber	Increased weight gain in pastoral steers including suckling steers and in spayed heifers and vealer calves. Improved feed efficiency and increased weight gain in lot-fed steers and spayed heifers	Nil
Compudose 400	43.9 mg oestradiol-17β	Silicone rubber	Silicone rubber	Increased weight gain in pastoral steers including suckling steers and in spayed heifers and vealer calves. Improved feed efficiency and increased weight gain in lot-fed steers and spayed heifers	Nil
Compudose G	60 mg trenbolone acetate 12 mg oestradiol-17β	Compressed pellet	Cholesterol	Improved growth promotion in pasture fed steers and heifers	Nil
Compudose G with tylan	60 mg trenbolone acetate 12 mg oestradiol-17β 29 mg tylosin tartrate	Compressed pellet	Cholesterol	Improved growth promotion in pasture fed steers and heifers	Nil
Progro H	200 mg testosterone propionate 20 mg oestradiol benzoate	Compressed pellet	Lactose	Improved weight gain in heifers	Nil
Progro S	20 mg oestradiol benzoate 200 mg progesterone	Compressed pellet	Lactose	Improved weight gain in steers	Nil
Progro TE-H	200 mg trenbolone acetate 20 mg oestradiol-17β	Compressed pellet	Lactose	Improved growth promotion and finishing of heifers	Nil
Progro TE-S	140 mg trenbolone acetate 28 mg oestradiol-17β	Compressed pellet	Lactose	Increased weight gain and improved feed efficiency in steers	Nil
Progro T-S	140mg trenbolone acetate	Compressed pellet	Lactose	Increased weight gain and feed efficiency in steers	Nil

Table 1 continued. Formulation of hormonal growth promotants registered for use in Australia

Product name	Hormone formulation (per implant)	Implant Type	Carrier Matrix	Label statement for use	Withholding period for beef production
Ralgro	36 mg zeranol	Compressed pellet	Lactose/boric acid	Increased rate of growth and improved efficiency of feed utilization in steer cattle	Nil
Revalor G	60 mg trenbolone acetate 12 mg oestradiol-17β	Compressed pellet	Cholesterol	Improved growth promotion in grass fed heifers and steers	Nil
Revalor H	200 mg trenbolone acetate 20 mg oestradiol-17β	Compressed pellet	Cholesterol	Improved growth promotion and finishing of heifers and steers	Nil
Revalor I	80 mg trenbolone acetate 16 mg oestradiol-17β	Compressed pellet	Cholesterol	Improved growth promotion in non-breeding cattle	Nil
Revalor S	140 mg trenbolone acetate 28 mg oestradiol-17β	Compressed pellet	Cholesterol	Improved growth promotion and finishing of steers	Nil
Synovex C	10 mg oestradiol benzoate 100 mg progesterone	Compressed pellet	polyethylene glycol	Improved weight gain in and heifer and steer calves	Nil
Synovex H	200 mg testosterone propionate 20 mg oestradiol benzoate	Compressed pellet	polyethylene glycol	Improved weight gain of heifers	Nil
Synovex S	20 mg oestradiol benzoate 200 mg progesterone	Compressed pellet	polyethylene glycol	Improved weight gain of steers	Nil
Synovex with trenbolone acetate	200 mg trenbolone acetate 28 mg oestradiol benzoate	Compressed pellet	polyethylene glycol	Improved weight gain and feed conversion efficiency in steers and heifers in confinement for slaughter under feedlot conditions	Nil

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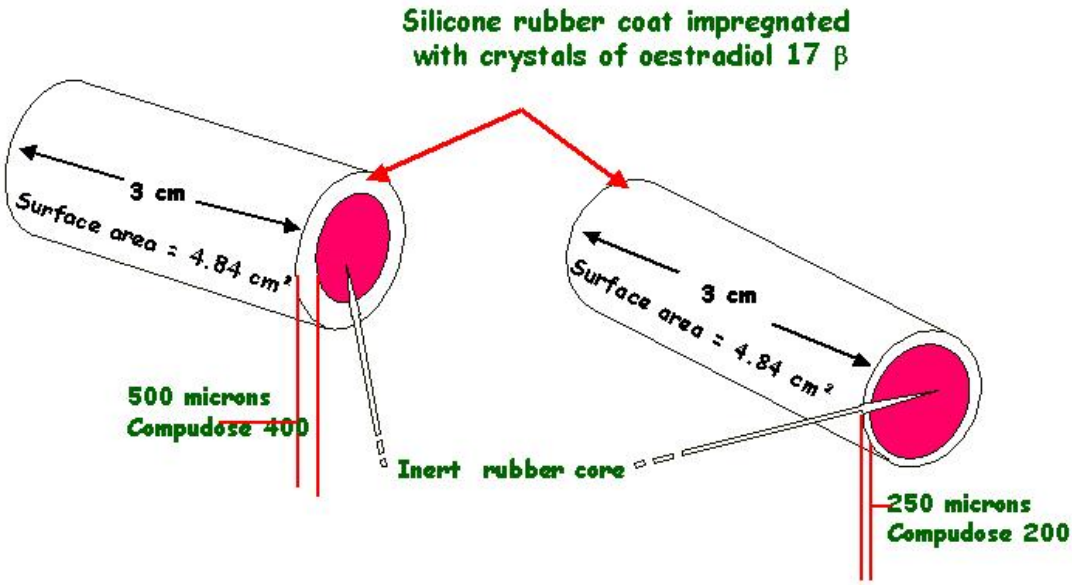

Figure 2. Diagrammatic representation of the architecture of two Compudose products with different functional lives.

The carrier matrices for the compressed pellet implants, listed in Table 1, are not authoritative and need to be interpreted with caution. The precise formulation of implants is 'commercial-in-confidence' to the manufacturing companies. Advice from the Australian Pesticides and Veterinary Medicines Authority (APVMA) is that the carrier matrices are not in the public domain. The data used in Table 1 were sourced mostly from information available on the internet [16] and from verbal information from one company.

It is a regulatory requirement that approved guidelines for use of the products be prominent on the label. Recommendations – like use only one implant per animal, do not use in animals under 6 weeks or 3 months or 6 months of age (depending on the product), do not reimplant sooner than 70 days after the last implant, are common. Notwithstanding these precautions and the fact that previous treatment of an animal with a HGP should be noted on the National Vendor Declaration at time of sale of the animal, there is little to prevent off-label use. The consequences of administering multiple implants to calves and older animals have been examined [17]. Treatment with up to 10 times the normal dosages of testosterone propionate and zeranol did reveal problems with infringement of the threshold values in edible tissues for human consumption. Off-label application of trenbolone acetate and oestradiol benzoate at three times dosage led to higher than threshold concentrations of hormone residues in livers of some animals while concentrations in muscle, kidney and peri-renal fat of all animals were not excessive. This experiment measured the accumulation of residues in tissues 56 days after treatment, presumably to test hormone residue concentrations at their near maximum values. While these data suggest a low risk of untoward consequences from double implantation, the practice should not be condoned.

Functional life of different implant formulations

For the purposes of this paper, the functional life of an implant is defined as the period of time for which the implant releases hormone. The duration of the anabolic response during which growth promotion occurs is a separate issue which will be considered later.

There is general agreement that the functional life of compressed pellet HGP implants is in the vicinity of 60-120 days [18,19,20,21]. The wide variation is probably the result of the different methods by which functional life is measured. Some studies measured the disappearance of hormones gravimetrically after the removal of the implant while others measured the concentrations of hormones in blood. The label of most compressed pellet implants carries the recommendation that animals should not be reimplanted within 70 days of the first implant which implies a functional life of about that length of time.

Blood serum or plasma hormone concentrations of implanted animals are characterised by a high initial peak in the first 1-3 days followed by a depletion curve that is generally similar to first order kinetics [22]. This is shown diagrammatically in Figure 3.

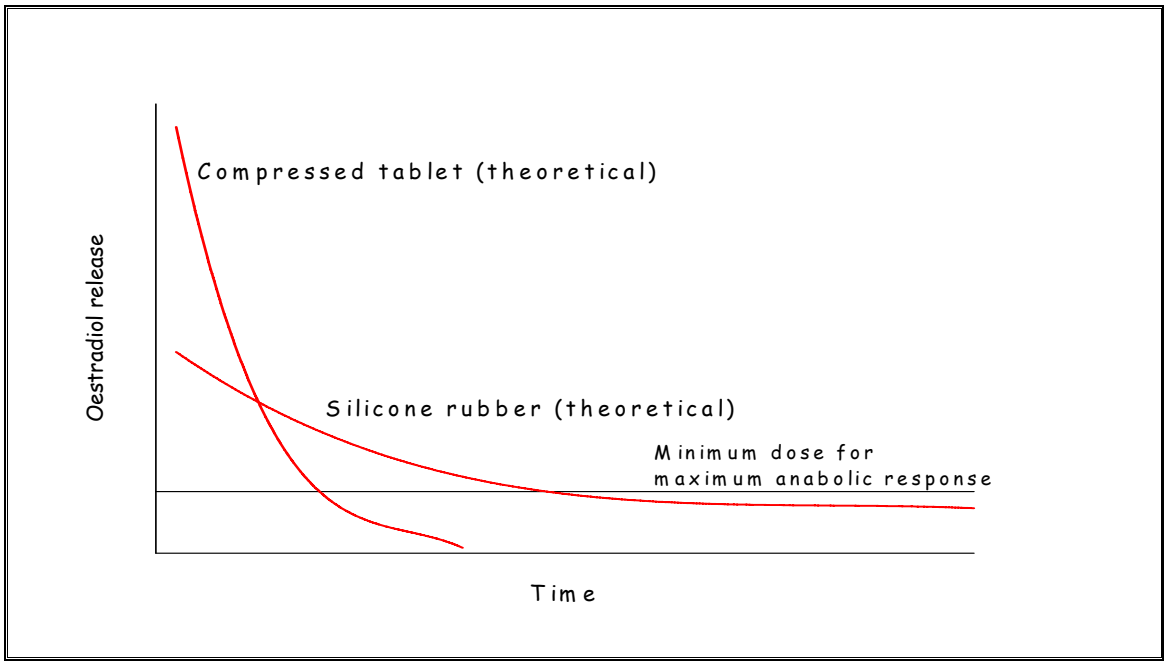

Figure 3. Theoretical release rates for compressed pellet and silicone rubber implant.

It is likely that there should exist a theoretical serum or plasma concentration of hormone below which growth promotion will not occur [1,22]. As yet, serum or plasma concentrations have not been established for any of the hormones and it may be that these thresholds are different for different classes of animal and different rates of gain. For example, a pay-out of 55 ug/d of oestradiol was suggested to maximise the growth rate of steers growing at 1.0 kg/d [23] but an oestradiol pay-out of 174 ug/d was optimal for steers growing at the faster rate of 1.3 kg/d [24]. In calves a release rate of only about 30 ug/d provided maximum growth rates [25].

The nature of the carrier and mixture of hormones in compressed pellet implants affect the release rate of hormones from the implant. Hormone release occurs through disintegration of the pellet and/or dissolution of the carrier matrix and exposure of the hormone to body fluids. Initially lactose was used as a carrier in compressed pellet implants because it is harmless to tissues and yields hard pellets [26]. However its high solubility led to rapid release of hormone from the pellet and a shorter functional life. Because it has a lower solubility than lactose, cholesterol is used to slow the rate of hormone release.

Mixing oestradiol with testosterone, trenbolone acetate or progesterone in compressed pellet implants results in a slower and more sustained release of the oestradiol than from pellets

containing only oestradiol [27]. Plasma concentrations of oestradiol were elevated for 91 days from a combination implant of oestradiol and trenbolone acetate and only 28 days [18] from a pellet containing only oestradiol. As all cholesterol based compressed pellet implants used in Australia contain a mixture of hormones, it follows that the functional life is towards the longer duration for this class of implant.

The formulation of silicone rubber HGP implants results in a pay-out of hormone that is at a slower rate and over a much longer period than compressed implants (see Figure 3). This type of delivery system is used in Compudose 100, 200 and 400 in which the only growth-promoting hormone is oestradiol-17β. The oestradiol is impregnated into the silicone rubber which serves as a reservoir for the oestradiol. The oestradiol then diffuses through the silicone rubber to the surface of the implant from where it is absorbed into the animal. The amount of oestradiol delivered each day is dependant on the surface area of the implant [25]. The functional life of the implant is determined by the thickness of the silicone rubber and hence the size of the reservoir for the oestradiol, provided all else remains constant. The dimensions of two silicone rubber implants with different hormone pay-out periods are shown in Figure 2. The implants have an initial burst of oestradiol over the first 28 days followed by a first order kinetic pay-out curve. The near linear portion of the curve indicates a pay-out of 50-60 ug/d, decreasing only very slowly with time [25]. This type of delivery system means that silicone rubber implants have a much longer functional life than compressed pellet implants. Serum oestradiol concentrations remained substantially elevated 378 days after administration of a 400 day silicone rubber implant, though the difference in concentrations between the implanted steers and the unimplanted controls was decreasing over time [28].

Duration of anabolic activity

There is general consensus in the scientific literature that compressed pellet implants do not stimulate anabolic activity beyond about day 140 after implantation [1,29]. There is evidence from a study which used increased nitrogen retention as an indicator of anabolic activity that pellets with a lactose carrier containing both oestradiol-17β and trenbolone acetate had a period of anabolic activity as short as 35 days. In contrast, pellets of the same formulation with cholesterol as the carrier had periods of anabolic activity from 80 to 105 days [26]. Implants containing trenbolone acetate give large growth responses, in the order of 30-60 %, during the first 28-35 days after implantation. The response then diminishes over a 120 day period to give a final overall response of 15 to 20 % [1]. On the other hand, oestrogen based implants do not seem to promote such an initial burst of anabolic activity, the growth response being only 5-10 % over the first weeks [1]. These potencies have all been determined in the USA with cattle on high-energy feedlot diets.

In Australia with cattle at pasture, the situation is somewhat clouded with respect to the period of anabolic activity, at least for implants containing trenbolone acetate. The label for Revalor G (60 mg trenbolone acetate, 12 mg oestradiol-17β) says that “improved weight gain can be expected 90-100 days post implantation in good quality healthy stock on good nutrition. The increased growth in this period should be maintained when measured at 400 days”. This implies an anabolic period of about 100 days and maintenance of the additional weight gain thereafter. Evidence to support this claim was presented to the APVMA by the company seeking registration. However the maintenance of an initial 100 day liveweight advantage is not universal. In an experiment with weaner steers implanted with 40 mg trenbolone acetate and 8 mg oestradiol-17β, the significant liveweight advantage at day 100 was eroded over the next 150 days so that by day 400 the liveweights of both treatment and non-treatment groups were similar [30]. It should be noted that the dose rates of the hormones used in weaners in this experiment were only two-thirds of that contained in the currently registered commercial products for pasture-fed cattle. These were the hormone doses recommended by the manufacturer of the implants as being suitable for steers of initial liveweight of about 200 kg. The experiment was conducted prior to the 60 mg trenbolone acetate and 12 mg oestradiol-17β product being registered for use in Australia. It was the same formulation as the 140 mg trenbolone acetate and 28 mg oestradiol-17β product in use at that time. The lower dose was achieved by implanting fewer pellets.

The sustained release of oestradiol from the type of silicone rubber implants currently used ensures a long period of anabolic activity. There is general recognition that silicone rubber implants promote anabolic activity for almost all of the period of 100, 200 or 400 days shown on the label of the product [16,28,29]. Further, there does not appear to be an appreciable attenuation of the anabolic response over time. In an experiment in which steers in continual positive energy balance were weighed regularly over 420 days, the growth rate response of steers implanted with the 400 day product was the same for the first and final 200 day periods [28].

Mechanism of action

There are different hormones with different roles in the metabolic functions of growth and reproduction used in HGPs. This section reviews their individual actions in growth promotion.

The biochemical and physiological means by which anabolic steroids promote growth in ruminants has been studied extensively over the last twenty-five years, yet there is still not a definitive mechanism, or mechanisms, which explain all the scientific observations. Some uncertainty possibly arises because some experiments studied the mechanism of action of implants that contain both an oestrogen and an androgen, while others considered the actions of oestrogens and androgens separately.

A number of hormones are involved in the regulation of normal growth. These include growth hormone, thyroid hormones, insulin, insulin like growth factor (IGF-1) as well as oestradiol and testosterone. Cattle have low endogenous oestrogen production compared to some other mammals and they respond well to supplementary oestrogen by increasing growth rate [9]. The magnitude of the growth response increases with increasing dose rate up to a threshold [25] implying an initial deficiency of endogenous oestrogen for maximum growth rate. Likewise, androgens in cattle are less active than in some other mammals; they have correspondingly lower androgen receptor concentrations in muscle and there is also a growth response to supplementary androgens [9]. The growth response to both oestrogens and androgens is mediated via intracellular receptors, directly in muscle as well as indirectly by increasing the circulating amounts of other growth promoting hormones [9].

The early explanation for the growth promoting effects of implanted oestrogens was a stimulation of activity of the pituitary gland resulting in additional growth hormone secretion. It is now known to be more complex because the growth promoting effects of exogenous oestrogen and growth hormone are additive [1] which suggests that oestrogens promote growth by means other than a simple increase in growth hormone secretion. The indirect actions of implanted oestrogens extend to increasing the concentrations of growth hormone receptors in liver and increasing IGF-1 concentrations in blood [31,32]. Increased IGF-1 concentrations have been linked to stimulation of muscle satellite cell proliferation and increased muscle growth [33,34]. It has been established that satellite cells are active in post-natal muscle growth by providing nuclei to the growing fibre in both pigs and cattle [35,36,37,38]. However as the animal matures, the total number of satellite cells decreases and a proportion of those that remain are quiescent [39,40]. The implication is that as an animal advances towards maturity, the declining activity of satellite cells and the decreasing muscle growth are linked. Reactivation of satellite cell activity by treatment with exogenous hormones might facilitate increased muscle growth. Implanted oestrogens are now thought to have a direct as well as an indirect action on the muscle cell [9]. Oestrogen receptors are present in cattle muscle though their concentration is many-fold less than in the uterus. Their physiochemical and biochemical characteristics match those of the uterine receptor [41]. Along with androgen receptors, they occur in numerous muscles of the body in a concentration in accord with the allometric growth of the muscle, providing evidence for the postulation of a direct action of oestrogens on muscle growth [42].

Trenbolone acetate is the androgen most commonly used in implants and it appears that its main action is directly on the cell. Trenbolone shows strong binding to the androgen receptor, the progestin receptor and the glucocorticoid receptor [43]. Its growth promoting potency is based on

both anabolic activity as an androgen and anti-catabolic activity as an anti-glucocorticoid. Trenbolone acetate has been shown to increase the rate of protein deposition through a small reduction in the rate of protein synthesis in muscle and a much larger decrease in the rate of protein catabolism [44,45]. In contrast, testosterone stimulates both protein synthesis and protein degradation [46]. It also, like the oestrogens but unlike trenbolene acetate, increases the circulating concentrations of growth hormone and IGF-1 [47], so probably has an indirect as well as a direct effect on growth promotion.

In cattle on a high plane of nutrition, the initial growth response to a commercial HGP implant containing both an oestrogen and trenbolone acetate is superior to that of an implant containing just an oestrogen. This is presumably the additive effect from two hormones with differences in the way they promote growth.

Growth response

The growth response (10-30%) to implanting cattle with HGPs is immediate and on a whole mob basis reasonably predictable. This is demonstrated in Figure 4 where a large number of experiments with grass-fed cattle and a number of commercial products are summarised. Each point on the graphs represents one experiment. The experiments were in northern and southern Australia and with both *Bos indicus* and *Bos taurus* cattle and their crosses. The results of many of the experiments are not in the public domain; the data having been made available on a confidential basis by the relevant companies. Most of the experiments were conducted on commercial properties under industry conditions. The liveweight gain data used to generate the figure were that during the functional life of the implant or the period of anabolic activity (see definition above). Only data from cattle treated for the first time with a single implant were used. The line on the figures shows the neutral situation when liveweight gain of the implanted animals equalled that of those not implanted. Also shown is a regression equation describing the relationship between the liveweight gains of implanted and non-implanted cattle. Though it needs to be viewed with substantial caution, it is included to demonstrate the predictability of the response through the very high r squared value and in some cases the “on average” magnitude of the growth response.

The caution in interpretation of the regression equations is because the data used were that of the means of treatment groups, not the individuals within the groups. Thus not all the variation between individual responses within the groups is accounted for. Notwithstanding this, the sheer number of cattle and experiments involved (68 for Compudose 200) does allow some conclusions to be drawn.

Figure 4 demonstrates that in almost all cases there was a positive growth response to implantation. The regression equations show that for the relatively short duration implants, Ralgro and Compudose 200, the additional liveweight gain of cattle on pasture was about 0.1 kg/d. The additional weight gain of about 0.1 kg/d is also what has been recorded in published scientific studies that were not used in the generation of the figures. It would be inappropriate to use data included in the generation of the relationships for comparison later. Therefore data from a number of peer reviewed publications were not included so valid comparisons could be made. In central Queensland with various breeds and breed crosses and at base liveweight gains between 0.3 and 0.6 kg/d, additional liveweight gains to treatment with Ralgro and Compudose varied between 0.10 and 0.19 kg/d, with all but one in the range of 0.10 to 0.14 kg/d [48,49].

The situation with the longer acting Compudose 400 is more complex (Figure 4(b)). The mean (± SEM) duration of the experiments reported was 364 ± 14.3 days so the vast majority of experiments were reliable tests of anabolic response over an extended period of about a year’s duration. As all the experiments were in northern Australia, a wet season with moderate weight gains and a dry season with low weight gains, weight stasis or even weight loss would have been involved. The regression equation in Figure 4 (b) predicts a liveweight gain advantage to implantation of 0.06 kg/d at a base growth rate of 0.3 kg/d and an advantage of 0.09 kg/d at a base

of 0.6 kg/d. This is in general agreement with the overall average of the 40 experiments which was 0.07 kg/d. This translates to an additional 28 kg over the 400 day life of the implant.

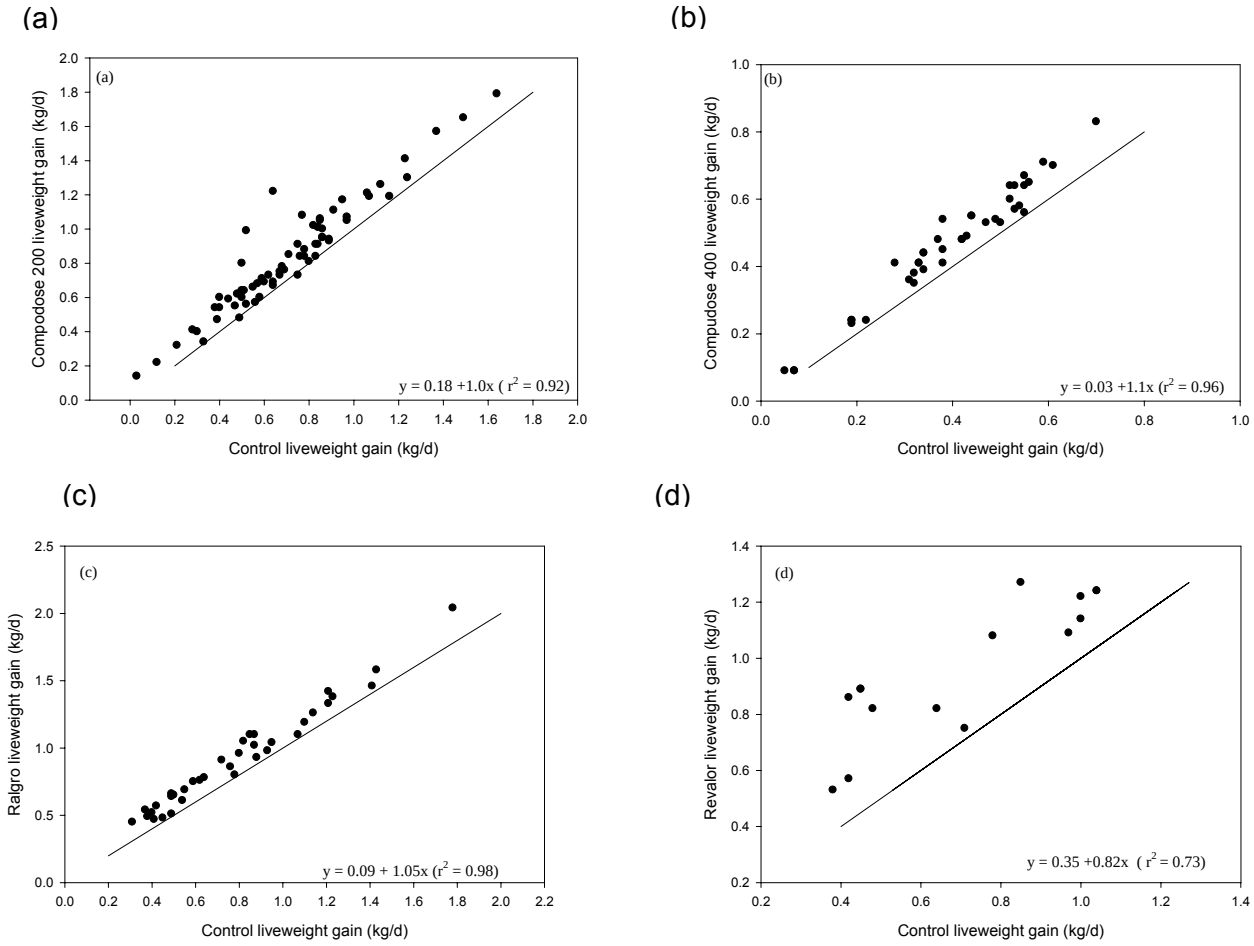

Figure 4[2]. The liveweight response in individual experiments with pasture-fed cattle implanted with (a) Compudose 200, (b) Compudose 400, (c) Ralgro, (d) Revalor. The straight line shows the situation of equality of liveweight gain between implanted and non-implanted cattle.

Again the liveweight average advantage in these experiments is similar to that reported in published experiments not included in the generation of the figure. In three experiments in Queensland, the liveweight advantage to steers implanted with Compudose 400 for at least 400 days was 0.05 to 0.06 kg/d [28,30,50]. However it should be noted that quite a different result was

[2] The data used in the generation of figure 4 were results from Australian experiments organised by or conducted by Elanco Animal Health and Virbac Animal Health or their associate companies. These results are not published in the scientific literature, but were kindly made available for this review. Other data were from:-

Hodge PB, Plasto AW, Round PJ, Smith PC, Aubrey JN, Mulder JC (1986). Effects of two growth promotants on liveweight gains in grain and grass-finished zebu crossbred steers
Proceedings of the Australian Society of Animal Production, **16**, 235.

Hunter RA (2000). Sustained growth promotion of pasture fed steers. *MLA. Final Report,* CS231.

Knights PT, Venamore PC (1985). Growth promotant review in Central Queensland. *Queensland Department of Primary Industries*, RQR85006.

MacDonald RN (1992). Trenbolone acetate/oestradiol as a wet season growth promotant for steers on low quality native pasture. *Proceedings of the Australian Society of Animal Production*, **19**, 418.

Sawyer GJ, Casey RH, Barker DJ (1987). Growth response of steer calves treated with zeranol, oestradiol-17β or progesterone-oestradiol benzoate implants before and after weaning. *Australian Veterinary Journal***, 64(12)**, 371.

Tudor GD, James T, Hunter RA (1992). Seasonal growth and carcass characteristics of grazing steers implanted with trenbolone acetate and oestradiol. *Australian Journal of Experimental Agriculture,* **32,** 683-687.

achieved in New Zealand with young steers constantly gaining weight at more than 0.7 kg/d. Over 266 days the liveweight advantage to those implanted with Compudose 400 was 0.13 kg/d [51]. This raises the possibility of similar responses, and responses equivalent to those with shorter acting implants, in southern Australia where base liveweight gains are generally much higher and more sustained during the year than those in the north.

There is general agreement in the scientific literature that at least on high energy diets, combination implants containing both an androgen and an oestrogen give an increased growth response to implants containing only an oestrogen for the first 100 days after implantation [1,52]. A comparison of Figure 4 (d) with Figures 4 (a), (b) and (c) suggests that this is also the case with cattle with low to moderate growth rate at pasture in Australia.

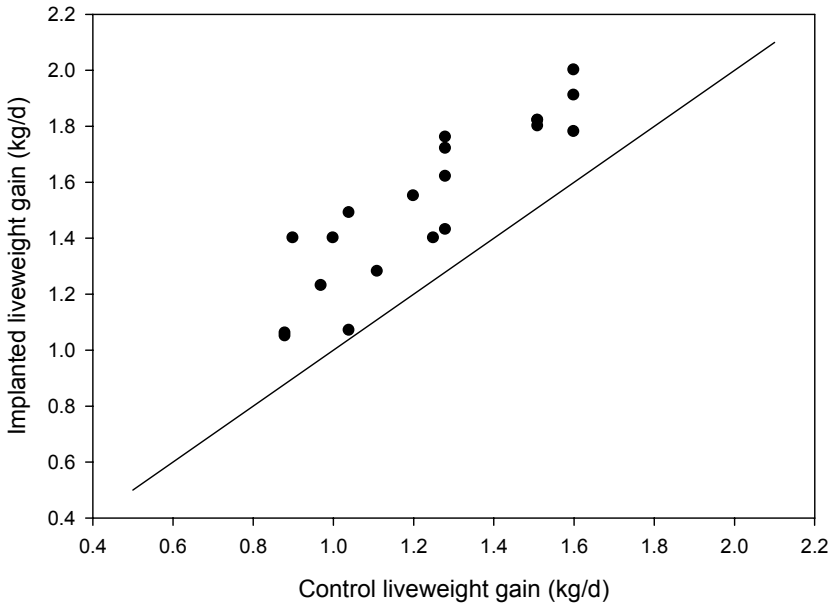

Figure 5[3]. The liveweight response in individual experiments with feedlot steers and heifers implanted with one of the following HGPs; Revalor S, Revalor H, Synovex S, Compudose 100, Ralgro. The straight line shows the situation of equality of liveweight gain between implanted and non-implanted cattle.

[3] The data used in the generation of figure 5 were results from Australian experiments organised by or conducted by Elanco Animal Health and Virbac Animal Health or their associate companies. These results are not published in the scientific literature, but were kindly made available for this review. Other data were from:-

Hoffman WD, Hearnshaw H (1996). Growth promotant (Revalor) increased liveweight gains while maintaining desirable carcase traits in feedlot finished steers. *Proceedings of the Australian Society of Animal Production*, **21**, 474.

Knights PT, Venamore PC (1985). Growth promotant review in Central Queensland. *Queensland Department of Primary Industries*, RQR85006.

Loxton I, Forster S, Barnes A, Ebbern K, Reid D, Doyle J (2001). Evaluation of hormonal growth promotants for the Brigalow Research Station feedlot. *Queensland Department of Primary Industries*. Final Report Q001004.

Sawyer GJ, Jennings MP, Barker DJ, Casey RH (1988). Response in liveweight and carcase gain to type of anabolic agent and repeat implantation of steers and heifers on feedlot. *Proceedings of the Australian Society of Animal Production*, **17**, 322.

Tudor GD, Sawyer GJ, Moyle PW (1996). Revalor H and dietary effects on growth and fat development in grain-fed early or late maturing heifers. *Proceedings of the Australian Society of Animal Production*, **21**, 431.

The data used to generate Figure 4 (d) was from experiments using Revalor G (60 mg trenbolone acetate, 12mg oestradiol-17β) and the higher dose Revalor S (140 mg trenbolone acetate, 28 mg oestradiol-17β). This was done because the reviewer was unable to source sufficient Australian data with Revalor G to draw meaningful conclusions. Although Revalor G is now recommended for grass-fed cattle, Revalor S was used commercially in cattle at pasture prior to the registration of the G product. The regression equation predicts a 0.24 kg/d response in growth rate at a base rate of 0.4 kg/d and a 0.20 kg/d response at a base rate of 0.8 kg/d. Some of these data were from experiments with calves between branding and weaning whose forage diet was supplemented with a high-energy diet from the dam. All data used were that from the first 100 days after implementation.

The liveweight gain responses from 18 experiments in Australian feedlot cattle are shown in Figure 5. Response to the various hormones and combinations of hormones are all on the one figure because of the paucity of information available. Many of the experimental results sourced did not have non-implanted controls and were a comparison of the various commercial products. Consequently these data were not included.

The seasonality of the Australian environment results in wide fluctuations in the nutritive value of pasture. The consequence is that cattle can take a number of years to reach target market weights. This is especially the case in northern Australia. Researchers at CSIRO Rockhampton investigated implantation strategies that achieved growth responses in addition to those achieved using a product that releases hormone over a 400 day period. Treatment of steers with 21 mg oestradiol-17β every 105 days for 420 days (4 implantations) resulted in a total liveweight gain of 279 kg compared with total gains of 251 kg and 230 kg for the 400 day product containing 44 mg oestradiol-17β (single implantation) and the non-implanted controls respectively [28]. A study that measured nitrogen retention as a measure of anabolic activity found that nitrogen retention was highest in the first weeks after implantation and attenuated towards the end of the 100 day period [10]. Presumably the additional hormone supply associated with the new implant re-boosted anabolic activity.

Sustained liveweight gains of steers for periods of up to 700 days by reimplantation with a series of oestrogenic and androgenic treatments and their combinations have been recorded. A response of 50 kg over non-implanted controls was achieved over a 400 day period by either alternate treatment of an oestrogen followed by an androgen on a 100 day rotation or repeat treatment with an oestrogen (total liveweight gains, 250, 300 and 293kg respectively for non-implanted and treated steers) [10]. In another experiment, repeat treatment with oestradiol-17β every 100 days achieved a growth response of 42 and 47 kg in steers finished for the Japanese ox market in a feedlot and on pasture respectively (total liveweight gains, 293 and 335 kg, 327 and 374 kg for non-implanted and implanted for feedlot and pasture finished respectively) [53]. Two treatments with 140 mg trenbolone acetate and 28 mg oestradiol-17β over 302 days resulted in a 37 kg liveweight gain advantage over non-implanted controls (total liveweight gains of 190 and 153 kg respectively) [54].

In the transfer of cattle from the grass-fed to the feedlot sector, the implant status of an animal may not be well-defined. If an animal has a residual functional implant, there is the potential for double dosing with consequences for behaviour in the feedlot, carcass and eating quality modification. The effects of HGPs on these will be discussed in later sections of the review. For growth rate, there is evidence [55] that greatest lifetime gains through the pasture and feedlotting phases are achieved with a progression through implants with low, moderate and high anabolic activity. For steers this could translate to using Ralgro, Compudose or Synovex C in the growing phase, Synovex S, Progro S or Revalor G in the backgrounding phase/early feedlotting phase, then Revalor S or one of the oestrogenic implants plus Progro T-S as a terminal implant in the late feedlotting phase. Such a strategy was confirmed when the results of 77 experiments involving 14,127 feedlot cattle were analysed [56]. Best growth rates were achieved with a second implant of an oestrogen plus an androgen. The same study also examined 30 experiments involving 5,489 heifers. There needs to be some caution with these results because of the small number of

experiments which included a reimplantation strategy. The best growth rates resulted from repeat implantation with an oestrogen or repeat implantation with the combination of both an oestrogen plus an androgen.

Treatment during periods of liveweight loss

There is no published information to suggest that the liveweight performance of implanted cattle is disadvantaged during periods of liveweight loss. This applies even with oestradiol treatment which acts through the growth hormone axis to promote growth. Increased growth hormone activity is consistent with an increase in metabolic rate and an increase in maintenance energy requirements. Steers treated with 20 mg oestradiol benzoate and 200 mg of trenbolone acetate were found to have slightly elevated fasting metabolic rates compared to non-implanted controls, though the difference was not statistically significant [57]. However undernourished steers treated with 24 mg oestradiol-17β had similar fasting metabolic rates and lost weight at a similar rate as non-implanted controls [49]. Similarly undernourished steers treated with up to 400 mg trenbolone acetate plus oestradiol 17-β in the ratio of 10:1 lost weight at about the same rate as non-implanted controls [58], so dose of the combination of hormones appears not to be an issue.

Large doses of trenbolone acetate alone (300 mg or more) do reduce the rate of weight loss in steers during periods of chronic under-nutrition [58,59,60] associated with a 10 % reduction in metabolic rate [61]. The product containing 300 mg of trenbolone acetate alone, Finaplix, is no longer registered for use in Australia.

Genetic selection for growth and response to HGP treatment

Using a variety of indicators, the overwhelming probability is that there has been no measurable diminution, or increase, in the growth response to HGP treatment associated with increased genetic selection for growth rate.

Since the first HGP product was registered for use in Australia about 30 years ago, there has been considerable genetic selection for improved growth rate in cattle breeding programs. Estimated Breeding Values (EBVs) for weaning weight, weight at 400 days and weight at 600 days are now commonly used in decisions on bull purchases in all environments. The question arises as to whether there is any interaction between increased genetic selection for growth and response to HGP treatment. This is almost impossible to test by direct scientific experimentation because it would involve comparing a group of modern cattle with a group that has undergone no selection pressure, including natural selection, for the last 30 years. The question can, however, be addressed using indirect or circumstantial evidence.

The previous section on mechanisms of action documents that HGPs stimulate growth by modifying a few select metabolic pathways. Genetic selection for growth rate generally takes a much broader but less well-defined approach. Animals that are heavier at the point of selection or have genes, as measured by EBVs, or gene markers that are associated with increased growth rate are used for breeding. There are many components capable of influencing growth rate, including feed intake, digestive efficiency, adaptation to the climatic environment, disease and parasite resistance, temperament, as well as a myriad of interrelating biochemical and physiological transactions. The vast majority of these are not substantially influenced by HGP treatment. For genetic selection to influence the action of an HGP, the metabolic pathways through which HGPs operate would have to be advanced to such an extent that no further advancement was possible. For example, cell receptors would have to be fully saturated continually for 100 days straight so no binding associated with exogenous hormone treatment could occur.

Genetically, survival is of higher priority than improvements to growth rate. During chronic under-nourishment, cattle can reduce their maintenance energy requirements by 25 % over 3 months [62] by reducing the amount of high metabolic activity tissues such as liver and gut. Despite this

genetically controlled device to reduce energy requirements and increase the probability of survival, chronically under-nourished cattle still reduce their energy requirements, measured by metabolic rate, a further 10 % when implanted with 300 mg trenbolone acetate [61]. Presumably the HGP treatment assisted the animals to reduce energy expenditure by involving a new method of energy reduction or increasing the activity of one that was already in use.

Further circumstantial evidence that the growth response to HGP treatment co-exists unchanged with genetic selection for growth lies in the lack of published information on the subject. A search of the scientific literature failed to identify one publication addressing the issue. Concurrent genetic improvement programs and refinement of implant programs are central to the beef production industry in the United States. The steady stream of scientific publications from that country continues to report growth rate and feed efficiency responses to HGP treatment that are still in the range that was reported twenty years ago.

Effects on feed intake and efficiency of feed conversion

A review of numerous feedlot experiments in the United States which included experiments with different implantation strategies concluded that the average increase in liveweight gain was 18 %, the average increase in feed intake expressed as kilograms per day was six % and the average increase in feed conversion efficiency was 8 %. [52].

An important question of biological and economic significance is whether the higher daily feed intake of implanted cattle is associated with their increased feed requirements due to increased liveweight or whether hormone treatment increases feed intake *per se.* The action of oestrogens in increasing the secretion of growth hormone, slightly increasing metabolic rate and consequently energy requirements for maintenance was discussed previously. Scientific investigations from the feedlot sector invariably report feed intakes in kilograms per day. However some studies provide sufficient information to allow mean feed intakes to be calculated on a per kilogram of liveweight basis. Although statistical analysis of the mean values from each experiment is not possible, reliable conclusions can be drawn. Over the number of experiments for which calculations were made, there was no trend for implanted steers or heifers to have higher feed intakes on a grams of feed per kilogram of liveweight basis than their non-implanted contemporaries [63,64,65,66,67,68]. This trend for similarity of intakes between implanted and non-implanted cattle was not affected by the crude protein content of the diet [68], the type of hormone formulation used [67] or the nature of the reimplantation strategy [64,65]. Consequently it is reasonable to conclude that implanted cattle eat more feed per day because they are heavier not because hormone treatment increases the drive for feed consumption.

This conclusion is consistent with results from experiments with steers gaining weight on forage diets in which feed intake per kilogram of liveweight was measured and found to be not statistically different between non-implanted control steers and steers treated with testosterone propionate [69] or oestradiol-17β [49].

For single implantations, the hormone formulations which result in the largest responses in growth rates are those which result in the largest improvements in feed conversion efficiencies. Combined implants of trenbolone acetate and oestradiol are associated with larger improvements than implants containing only oestradiol [52,67]. However with multiple implantation strategies, irrespective of the type of hormones used, there appears to be no evidence that one strategy is superior to another in improving efficiency [64,65]. Furthermore, repeated implantation with oestradiol during the grow-out phase at pasture did not impair the improvement in feed conversion efficiency of cattle given implants of oestradiol alone or implants of oestradiol plus trenbolone acetate during feedlot finishing [64].

The improvements in feed conversion efficiency with HGP treatment are of commercial significance for feedlots because the feed costs per unit of liveweight gain are decreased. Calculations using published figures for the energy requirements for a growth rate of 1.25 kg/d [70],

assuming an eight % improvement in efficiency from implantation, show the following for a grain-based diet of 12MJ/kg dry matter:

- The feed requirements for a steer entering the feedlot at 300 kg liveweight and gaining 100 kg are 646 kg and 594 kg for a non-implanted and an implanted animal respectively.
- The feed requirements for a steer entering the feedlot at 400 kg and gaining 250 kg are 1,692 kg and 1,556 kg for a non-implanted and an implanted animal respectively.

Effects on carcass composition

The anabolic actions of HGPs result in a greater proportion of the metabolisable energy intake being partitioned towards protein rather than fat deposition. This means the energy content per unit of liveweight gain at comparable stages of growth is less in implanted cattle and they are heavier at common body composition with non-implanted cattle [71]. The corollary is that HGP-treated cattle are leaner at any given bodyweight. The increased carcass leanness at any given liveweight is usually from 5-8 % [1]. Whether there are measurable differences in carcass composition at slaughter, depend on a number of factors such as the type of implant used, the duration of the implant program, the stage of growth at which the cattle are implanted and the maturity type of the cattle involved.

HGP treatment also increases frame size [72,73,74]. Thus at any given intermediate weight, implanted cattle are more distant from their mature liveweight and mature body composition than comparable non-implanted cattle. This has implications for the scientific interpretations of experimental results because data are often adjusted for, and comparisons made, at the same carcass weight. When this is the case, the comparison is between more mature non-implanted cattle and less mature implanted cattle. Thus it is not surprising that implanted cattle are often found to be leaner. This is of commercial significance as cattle are often traded at a specified market weight, not a specified degree of maturity.

The hormone composition of the implant has an influence on the relative deposition rates of fat and protein and on the differential growth rates of different muscles. Bulls produce leaner carcasses than steers with lower proportions of subcutaneous and intramuscular fat [63]. Similarly, implants containing testosterone or trenbolone acetate also produce leaner carcasses when comparisons are made at the same end date. Though there is increased musculature in all areas of the carcass, there is an added tendency for increased weight of neck muscles as is the case with bulls [75]. Feedlot heifers treated with 200 mg trenbolone acetate and 20 mg oestradiol-17β also had increased meat yield, primarily in the lower value cuts, and reduced fat deposition compared to non-implanted controls [76]. Oestradiol, whether implanted once or a number of times, generally has a lesser impact on carcass fatness in cattle slaughtered at commercial bodyweights [28,51,53,56]. This implies that oestradiol does not modify carcass composition to the same extent as the androgens (testosterone and trenbolone acetate).

There is a paucity of experimental information on the body compositional changes that occur in response to androgenic implantation of pasture-fed cattle slaughtered at commercial end-points in Australia. Repeated treatment with 140 mg trenbolone acetate and 28 mg oestradiol-17β at regular intervals for 12 months reduced P8 fat depth from 12 mm in non-implanted steers of 584kg final liveweight to 8 mm in implanted steers of 604kg final liveweight [54]. The 140 mg trenbolone acetate product has now been replaced by a 60 mg product for cattle at pasture so it is possible that the lower dose product would have a smaller effect on carcass fatness.

Long term (with one implant for 400 days) and repeated (every 100 days for up to 700 days) treatment with oestradiol-17β had minimal impact on carcass fatness of cattle finished on pasture or in a feedlot and slaughtered at weights corresponding to the domestic, Korean and Japanese specifications when the comparisons were made at the same carcass weight [28,53]. Weight of retail primals and eye muscle area were also unaffected by the very aggressive and non-commercial oestradiol treatment. At slaughter, the implanted animals were heavier and produced more beef

but this was associated with increased carcass weight rather than a differential increase in proportion of muscle.

The stage of growth and the maturity type of the cattle are likely to affect the response to body compositional change to implantation. These are discussed in some detail in the next section. Implantation of young cattle, especially late maturing genotypes of high mature bodyweight is likely to delay the onset of significant fat deposition. This can be of commercial significance for markets which require a specified fatness at bodyweights well below mature bodyweights. In some circumstances implanted cattle, especially those treated with trenbolone acetate or testosterone may attain market weight without the desired degree of fatness.

The effect of HGPs on marbling is confusing. There are many conflicting reports on the effect of various implant strategies from the United States feedlot sector. This confusion possibly arises through differences in implant status of cattle prior to the experimental phase in the feedlot, and differences in the lengths of exposure to hormonal treatment during finishing on a high-grain diet. There is general agreement in the scientific literature that oestrogens alone, even repeat treatment, have minimal effect on marbling score [73,77]. Even the aggressive, but non-practical strategy of implanting cattle every 100 days with oestradiol-17β from weaning through to finishing at pasture or in a feedlot did not modify intramuscular fat content when comparisons were made at the same carcass weight [53]. While it is clear that the degree of marbling is not increased by HGP treatment, the implants most likely to reduce marbling score are those containing trenbolone acetate combined with an oestrogen rather than those with just an oestrogen. The likelihood is increased when the combination implant is administered during early periods of growth and when treatment is repeated by a second such implantation during the feedlot phase [78]. There is evidence to suggest that intramuscular fat deposition begins as early as 4-12 months of age [79,80]. Androgenic treatment during this period is likely to retard the onset of fat deposition in muscle. Using an implant like an oestrogen alone during the early life of an animal, or no implant, before a terminal implant of trenbolone acetate and an oestrogen decreases the likelihood of marbling being reduced [81]. An histological and biochemical study of intramuscular fat cell growth has led to the suggestion that the combination implant does not have a direct effect on intramuscular fat deposition [82]. The effect is indirect through a dilution of the same amount of fat in a larger muscle [83].

Treatment of early and late maturing cattle

There are very few direct comparisons of the response to HGP treatment by cattle of different maturity type. Those that are available are consistent with the principles described above. HGP treatment increases frame size and mature bodyweight. Thus HGP treated cattle are heavier when they achieve the same body composition/degree of fatness as comparable non-implanted controls. At any given liveweight, late maturing genotypes are in a more anabolic growth phase than early maturing breeds as more protein relative to fat makes up the composition of the body gain. HGP treatment increases the intensity and duration of the anabolic activity. The deposition of unit weight of muscle requires less dietary energy than deposition of unit weight of fat so liveweight gains are generally higher earlier in an animal's life. This means that for animals fed *ad libitum* on good quality diets, late maturing European types could be expected to grow faster for a longer period of time than earlier maturing British types. Implanted European types in the active protein deposition phase of growth could be expected to have a greater response in growth rate to HGP treatment than early maturing types, where fat is a larger component of the body gain.

This theoretical hypothesis was at least partially validated in an experiment in Western Australia in which the liveweight response to treatment with 200 mg trenbolone acetate and 20 mg oestradiol was 26 % for 130 days feeding in heifers with European sires compared to 7 % response in Angus heifers fed for 94 days [84]. The different feeding period was because slaughter was at a target P8 fat thickness of 10mm. The weights at which the backfat thickness was reached was 387 kg for non-implanted Angus, 403 kg for implanted Angus, 409 kg for non-implanted European crossbreeds and 443 kg for implanted European crossbreeds; thus demonstrating the heavier

weights at which cattle, implanted with the hormones described above, attained the same body composition as non-implanted controls.

The results of 43 published independent experiments were combined in a meta-analysis aimed at relating maturity type and HGP status to carcass characteristics [85]. Neither maturity type nor implant status affected dressing percentage at any given commercial slaughter weight. Area of the *longissimus.dorsi* muscle was greatest in implanted, late maturing types and smallest in non-implanted early-moderate maturing types. Backfat thickness was in the reverse order to muscle area; non-implanted early maturing, implanted early maturing, non-implanted late maturing and the implanted late maturing cattle having the least depth of cover. These results are also consistent with the theoretical considerations and the results of the experiment in Western Australia [84].

Effects on meat eating quality

There has been considerable research interest over the last decade on the effect of HGP treatment on the eating quality of beef. In the early years of interest, there was uncertainty about whether there was, or was not, a negative effect and if there was, its magnitude. Now that larger data sets from experiments designed specifically to measure the effects of various hormonal treatments on eating quality are available, it is clear that the effect of implantation with growth promoting hormones is negative. The recent evidence also shows that reported HGP effects on tenderness and eating quality measures vary between studies, are often small and difficult to measure and are influenced by the number and type of HGPs used, animal breed and duration and type of post-slaughter treatment such as ageing. The following section details how our understanding of this commercially important issue has evolved over time.

It is suggested that the initial confusion surrounding HGPs and their effects on meat quality was associated with: 1) the way eating quality was measured; and/or 2) the variability of individual measurements on meat samples from the same muscle from animals in each treatment group; and/or 3) the relatively small sample size. The subjective measurement of eating quality using taste panels probably results in more variability around a mean value than measurements such as growth rate which are measured objectively, usually on more than one occasion. Additionally variability is probably introduced by differences in individual animal reaction to pre-slaughter handling and post-slaughter processing.

For example, in one experiment [53] with almost 20 animals in each of 4 treatment groups, the standard errors of the means for subjectively assessed eating quality were in the range of 5.0-6.3 % of the means compared to standard errors in the range of 3.9 -5.3 % of the means for growth rates. HGP treated steers had growth rates 14-16 % higher and eating quality scores of the striploin 9-12 % lower than the respective values for non-implanted controls. When these data were analysed statistically, the treatment differences in growth rate were statistically significant and treatment differences in eating quality were not. Thus to determine scientifically treatment differences in eating quality, more animals per treatment group would be required than in experiments where the major focus is measurement of objectively measured characteristics such as growth rate, carcass weight and subcutaneous fat thickness. This experiment reported the results of only the first calf drop in a larger study involving two calf drops. When the results from the second calf drop were included in the analysis and numbers of samples assessed for taste panel tenderness increased from 69 to 234, the negative effect of the HGP treatment on eating quality became statistically significant [86].

A search of the scientific literature for experiments which measured both growth rate and eating quality found that it was the norm for the positive response in growth rate to be larger that the negative response in objectively measured tenderness or subjectively assessed eating quality. Likewise, the variation around the mean growth rates was less than the variation around the mean tenderness and eating quality values [28,30,51,65,87]. This evidence suggests that experiments with larger sample sizes are required to demonstrate statistically significant differences in eating

quality compared to statistically significant differences in growth rate. As many of the experimental reports in the scientific literature were designed to measure the effect of HGPs on production characteristics with eating quality as an ancillary measurement, with hindsight it is not surprising that the eating quality effects were equivocal.

A review in 2002 concluded that HGPs have subtle, if any, effects on tenderness measured objectively or subjectively [88]. This investigation drew its conclusions from the results of over 30 experiments. The approach taken was to view each experiment independent of other experiments. Many of the experiments reviewed reported a numerical difference which was not statistically significant or no difference at all. As there was no real evidence of a recurring statistically significant effect, a conclusion of no effect was reached.

An alternative approach to the analysis of multiple experiments is the use of meta-analysis. This methodology provides more statistical power than the analysis of each experiment in isolation from other experiments. It is a quantitative mathematical procedure which is essentially an analysis of the combined statistical analyses of a number of experiments. It links experiments and in so doing increases the sample size which addresses the variability issue discussed above. A recent meta-analysis [89] provides evidence that HGP treatment leads to a reduction in beef tenderness of the longissimus dorsi muscle, measured objectively or subjectively. Interestingly both investigations [88,89] used many of the same published papers as a source of data but came to different conclusions because of the methodologies used.

Another reason for the lack of clarity about the effect of growth promoting hormones on eating quality has been the tendency to describe all treatments as HGP treatments, irrespective of whether treatment is with a single hormone or a combination of hormones administered only once or repeatedly. Some implant strategies might result in minor differences which are difficult to detect, while other strategies with a larger effect are more easily demonstrated. Both the experiment by experiment investigation and the meta-analysis appeared to reach conclusions on a general HGP effect without differentiating between the effects of individual hormones and different implantation strategies.

Over the last few years, it has become clear that combination implants of trenbolone acetate and oestradiol and testosterone propionate and oestradiol and multiple implants of all hormone formulations are associated with reduced tenderness and reduced eating quality of non-aged and aged steaks compared to non-implanted controls [86,89,90]. However the scientific literature does not appear to have considered the extent to which oestrogenic and androgenic hormones individually influence tenderness and eating quality of meat; probably because trenbolone acetate and testosterone are rarely implanted without an accompanying oestrogen in a combination implant. Also much of the early eating quality investigations were conducted in the United States where cattle are usually finished in feedlots and the majority are given a combination implant at least once during the finishing period.

There is recent evidence that the individual effects of trenbolone acetate and oestradiol in combination implants appear to be additive in increasing meat toughness and with repeat implantation there is a positive linear relationship between cumulative combined dose and toughness [91]. The move to whole of life implant programs and the increase in the aggressiveness of these programs, especially with feedlot finishing and use of combination implants, has brought increased attention onto the interaction of HGPs with eating quality.

The effect of commercial use of implants containing only oestradiol on meat eating quality has not been adequately addressed. It is known that repeated treatment with 20 mg oestradiol-17β every 100 days does lead to reductions in eating quality [86]. Such an aggressive strategy is unlikely to be used commercially in Australia. The Australian grass-fed industry, especially in northern Australia, has a heavy reliance on long-acting, silastic rubber implants containing only oestradiol. Steers are often implanted at branding or weaning with a 200 or 400 day implant and then implanted again

with one of these implants when the anabolic activity associated with the first has ceased. The cumulative lifetime dose of oestradiol would not usually exceed 100 mg.

In most of the Australian experiments in which there has been a statistically significant effect of hormone treatment on eating quality, combination implants of an androgen and oestradiol have been used. A single implant of either 140 mg trenbolone acetate and 28 mg oestradiol-17β or 200 mg trenbolone acetate and 20 mg oestradiol-17β resulted in a significant reduction in eating quality of non-aged steaks in steers and heifers respectively [90]. The meta-analysis of Watson [89] which also found a statistically significant negative effect of HGP treatment used the data sets available at the time which were mostly from feedlot experiments and which were dominated by those with multiple implantations and/or use of a combination of hormones as the terminal implant.

Another experiment [92] investigated the effect of various implant strategies during the grow-out phase on pasture in northern Australia followed by use of a combination implant during feedlot finishing. The lifetime cumulative dose of hormones varied between 56 mg oestradiol-17β and 60 mg trenbolone acetate and 84 mg oestradiol-17β and 200 mg trenbolone acetate and included a treatment of 52 mg oestradiol-17β and 260 mg trenbolone acetate. There were no significant differences between the various implant strategies, possibly associated with the small numbers in each treatment group (>15 for HGP treated groups). When all the HGP treatment were combined into one group, the negative effect of treatment on eating quality was statistically significant.

Circumstantial evidence suggests that implantation with oestradiol alone, as it is used commercially in Australia, has a lesser effect on eating quality than implantation with combinations of oestradiol plus androgens. The evidence can be summarised:

- One large study with 2,748 steers reported that untrained taste panellists could not detect any difference in eating quality between steaks, aged 21 days, from non-implanted control steers and steaks from steers implanted twice with 20 mg oestradiol benzoate for the 210 days before slaughter. On the other hand, trained panellists could detect the small difference that was evident from objective shear force measurements [93].
- There was no statistical difference in shear force values (6.3 kg and 5.9 kg for control and treated respectively) when steers (n = ~30 per treatment group) were administered 20 mg oestradiol-17β in the wet season in each of two consecutive years [30].
- There was no statistical difference in shear force values (6.3 kg and 6.2 kg for control and treated respectively) when steers (n = ~ 30) were administered 20 mg oestradiol-17β in the wet season followed by 44 mg oestradiol-17β 100 days later in each of two successive years [30]. In this and the preceding comparison, the shear force values were higher than those associated with acceptable tenderness. Factors external to treatment may have been involved and these may have masked treatment differences.
- There was no statistical difference in subjective assessments of tenderness and eating quality when steers (n = 240 for control and 235 for treated) were implanted with 20 mg oestradiol-17β every 100 days from soon after weaning until slaughter. The steers were prepared for the domestic, Korean and Japanese markets and had from 2-8 implants [94]. It should be noted that when data from the same data base of the Cooperative Research Centre for the Cattle and Beef Industries were analysed by other scientists, the difference between implanted and non-implanted steers for the subjective assessment of tenderness was statistically significant, driven largely by the magnitude of the reduction in tenderness in the straightbred Brahmans compared to the other breeds (see below) [86**Error! Bookmark not defined.**]. It should also be noted that such an aggressive implant strategy is unlikely to be used in commercial practice in Australia. Although both analyses used data from the same experiment and from the same data base, there is no way of knowing whether the particular data sets were exactly the same. In addition, the statistical models used may have been different.

- There was no statistical difference in shear force values when steers (n = 17 for control and 16 for treated) were implanted once with 44 mg oestradiol-17β (5.1 kg and 5.5 kg for controls and treateds respectively) [28].

However, the definitive experiments to quantify the relative impact of different implantation strategies typically used in north Australian grass-fed production systems have not been conducted.

Treatment with both oestrogenic and androgenic growth promoters results in advanced skeletal maturity [30,95]. This is seen in higher ossification scores at slaughter. This effect of HGPs in advancing physiological maturity of cattle has implications for the assessment of eating quality as some predictive models use ossification, notably increased ossification score, as an indicator of reduced eating quality. The degree to which skeletal maturity is advanced is influenced by the number and potency of the implants administered [96].

There is now clear evidence that post-mortem aging helps mitigate the detrimental effect on eating quality resulting from mild or moderately aggressive HGP implant programs. The extent of improvement in eating quality of HGP treated meat is muscle dependent, the magnitude of improvement being proportional to the aging rate of the muscle [90]. On the other hand, the muscles with the greatest rates of aging like the striploin are also the muscles where the negative effect of hormone treatment is greatest in the non-aged state and where the improvements from aging are greatest [97]. For example in this experiment, 21 days aging of the striploin resulted in steaks with shear force values not significantly different from non-implanted controls. The steers and heifers had each been implanted once with 140 mg trenbolone acetate plus 28 mg oestradiol-17β or 200 mg trenbolone acetate plus 20 mg oestradiol-17β respectively. With a more aggressive strategy of two trenbolone acetate/oestradiol implants in the finishing period, striploin steaks aged 21-28 days exhibited a substantial improvement in tenderness and were in the range where consumers would class the meat as tender (~ 3.5kg) [91]. However it should be noted that steaks from non-implanted steers also underwent similar substantial improvement in tenderness with aging and after 28 days were still objectively measured as more tender than steaks from implanted steers, though the difference was not statistically significant.

One study also found an interaction between genotype and oestradiol-17β use on meat eating quality [**Error! Bookmark not defined.**]. This study subjectively assessed tenderness of non-aged samples from the striploin in response to repeated implantation with 20 mg oestradiol-17β for three different genotypes. The reduction in tenderness of steaks from straightbred Brahmans (n=15) was 13.4 units compared to 5.3 units for F1 Brahman x Santa Gertrudis (n=9) (69 % Brahman) and a mean of 3.4 units for three F1 Brahman x *Bos taurus* crosses (n=85) (50 % Brahman). The reduction in tenderness compared to non-implanted controls was statistically significant for the straight bred Brahmans but not for the crossbreds.

Meat and Livestock Australia through Meat Standards Australia have developed a computer model which is used to predict eating quality of meat from easily measured characteristics of the animal, its husbandry and its carcass. Factors likely to affect final eating quality are taken into account and the ranking modified accordingly. The approach is risk averse and negative factors such as HGP status receive a muscle specific penalty commensurate with assured eating quality. The HGP penalty ranges from 8 MSA scores (MQ4) for the striploin aged for 5 days (5 points when aged for 21 days) to zero for muscles like the oyster blade.

HGP use does not prevent a carcass from MSA grading but will affect the MSA score achieved for the different muscles. For muscles that without HGP treatment would be near the bottom score for an MSA score (e.g. MSA 4), the additional penalty of having an HGP might move them to a lower grade (e.g. MSA 3) or prevent an MSA grade altogether (ungraded).

For simplicity of operation and lack of more specific information, the scheme does not differentiate between different implant formulations, single or repeat implantation or stage of growth of hormone treatment. An animal treated once between branding and weaning is treated the same as an animal subject to a whole of life implant program.

Effects on fertility of breeding females

The labels of most of the products registered for use in Australia with heifers carry the warning that the product should not be used in breeding females. This recommendation is sound because both oestrogenic and androgenic growth promoting hormones can impair ovarian development and function, and mammary gland development.

Possibly the only instance where treatment to promote growth might be administered without some negative consequence to reproductive capacity is single treatment of heifer calves on a high plane of nutrition with an oestrogen in the first few months of age [98,99]. Provided there is sufficient time for compensatory ovarian development to occur, the heifer will reach puberty at the normal time. However if they are not on a very high plane of nutrition, puberty is likely to be delayed. The variability of the Australian climate and its effect on nutritive value of pastures would preclude this strategy from being commercially attractive. The degree of impairment to reproductive function in all other cases depends on the type and dose of hormone administered and the age and/or physiological state of the heifer or cow.

Treatment of female calves with oestrogenic growth promotants increases pelvic area [99]. This might be attractive if it was associated with increased ease of calving, but unfortunately the increase in pelvic area relative to non-implanted controls has disappeared by calving, regardless of time of implantation [100,101,102].

There is clear evidence that implantation of young heifers, older than the calves in the particular set of circumstances described above, with oestrogenic hormones delays the onset of puberty [98,99,103] and that increasing the dose of hormone exacerbates the delay [104] through retarded development of ovarian and uterine tissue [105 cited by 99,104].

Conception can be delayed slightly with single treatment of young heifers [106] or reduced with repeated implantation [98].

Oestrogens are involved in normal development of the mammary gland in the post-pubertal heifer. Additional oestrogen supplied in an implant may have a stimulatory effect on duct development but may cause abnormal alveolar development [107]. In his review, Hargrove concluded that oestrogen treatment resulted in increased mammary tissue development (especially teat length) and increased vulva length [99] but presented evidence that milk production was not affected irrespective of whether the heifer is implanted before or during pregnancy. On the other hand, there is a report from New Zealand that a single, pre-weaning treatment of heifer calves with oestradiol-17β subsequently resulted in their own calves being about 16 kg lighter than calves from the non-implanted control contemporaries at weaning [106]. This was considered to be associated with a serious impairment of milk production in the first few weeks of lactation.

There is strong evidence that treatment of heifers with androgens is not conducive to peak reproductive performance. Treatment of females with testosterone or trenbolone acetate at much higher doses than are currently used in commercial implants has caused the cessation of ovarian activity for 100 days [108,109] delayed the onset of puberty [99], delayed first ovulation by 77 days [110] decreased calving rate and calf birth weight [111] and increased rate of abortions [112]. In the latter study, 40 % of cows in early pregnancy aborted after being injected every second day with 250 mg of testosterone propionate for 20 days. Commercial implants for heifers only contain 200 mg of testosterone propionate which enters the blood stream of the animal in small quantities over about 100 days. Injecting 250mg every second day was massive dosing compared to commercial implantation.

These consequences of treatment with high doses of hormone are listed to give the direction, if not the magnitude, of the physiological consequences of using implants containing androgens with females that may enter the breeding herd.

Repeat treatment of weaner heifers with a commercial product containing 200 mg testosterone propionate and 20 mg oestradiol benzoate was shown to decrease ovarian or follicular development [113]. This impairment may explain the 22 and 17 reduced calving rate in first and subsequent second calf heifers respectively when they were implanted with the same hormone combination on three occasions at 90 day intervals soon after weaning [114]. In this experiment mating for the first time did not commence until 290 days after the final implantation. Treatment of heifers at the start of mating with 300 mg trenbolone acetate decreased calving rate by 46 per cent [115].

Sometimes in Australia the pregnancy status of a cow is not always known and it is possible that a pregnant cow might be implanted with the objective being to increase growth rate before slaughter. For a cow in mid to late pregnancy, the ovary is relatively dormant and the pregnancy is maintained by the large amounts of hormones produced by the placenta. In this situation, it has been shown that the small amounts of additional hormone from an implant have a relatively minor effect on reproductive function. In an experiment in which the pay-out period of an implant containing 200 mg trenbolone acetate and 20 mg oestradiol-17β roughly coincided with the last 3 months of pregnancy, there was no effect of treatment on calf survival before or after birth [116]. There was some partitioning of ingested nutrients towards maternal tissues rather than calf growth in utero. Cows gained an additional 0.1 kg/d and calves were 3 kg lighter at birth. Milk yields appeared not to be affected as calf growth rates in the first 8 weeks of lactation were similar in both treatments. Fertility at the next mating was also unaffected by implant treatment.

Implant strategies and implant programs for sustained growth promotion

HGPs were first registered for use in cattle in the northern hemisphere where they were used as finishing agents. Cattle were implanted with a short-life implant about 3 months before slaughter. In these production systems, weaning weights were high and cattle were routinely slaughtered well before two years of age. The three months of hormone assisted growth represented a sizeable proportion of an animal's post-weaning life. The seasonality of pasture growth in Australia, especially northern Australia, results in cattle needing to have years, not months, of post-weaning growth to reach slaughter requirements. Consequently it would be advantageous in some situations if growth promotion could be sustained over years rather than just months.

Previous sections of this review have discussed the effects of HGP treatment on growth rate, carcass composition and eating quality. These effects need to be considered in relation to the aims of the beef production business before the decision whether or not to use HGPs is made. Once the decision to use HGPs is made, the implant program should be planned with the end beef product, both quantity and quality in mind. For example, if cattle with a genetic propensity for leanness are being prepared for a market that demands a generous fat cover on the carcass, it might not be prudent to use a hormone which promotes leanness in the final implant.

There are some general principles that can be applied to the design of implant programs [30]. The science behind them is outlined in the preceding sections of this review.

- Greater responses in liveweight gain are achieved when cattle are in continual positive energy balance than when they experience periods of liveweight stasis or weight loss.
- The more frequently cattle are treated with a new implant the greater the overall response in liveweight gain.

- Once an implant program has commenced, it should be continued through until slaughter if growth response is to be maximised.
- Sustained growth promotion can be achieved through repeat implantation with oestrogenic hormones or by alternate treatment of an oestrogen and a combination implant of an oestrogen plus an androgen.
- Repeat treatment with implants containing an androgen may reduce carcass fatness, increase forequarter development and result in downgrading of carcasses at slaughter.
- Oestrogenic treatment, even repeat treatment, does not modify carcass composition *per se*. Cattle attain mature carcass composition at higher mature liveweights. They may however be leaner at intermediate liveweights
- Repeated implantation, especially when usage of one or more combination implants occurs, results in a reduction in eating quality. Treatment with only one, or perhaps, two oestrogenic implants in the final years of finishing may have a lesser negative impact on eating quality.

The practicalities of managing a beef production enterprise probably mean that compromises need to be made between the scientifically optimal implant programs and commercial reality. Further, the current uncertainty of rainfall patterns compounds the situation, as high quality nutrition in certain seasons now cannot be relied upon.

In northern Australia, calves are usually weaned towards the end of the growing season and before the start of the long dry season. The growth rate that calves achieve on Brahman and Brahman cross dams is probably higher than any subsequent growth rate on pasture [10,117]. Implantation of steer calves with an implant containing oestradiol and trenbolone acetate at branding, several months before weaning, would result in a growth response in the order of 0.2 kg/d (see Figure 4 (d)). If this was the strategy, reimplantation at weaning would need to occur, perhaps with a long acting (200 day plus), silastic rubber implant containing oestradiol-17β to cover the animals through the dry season. With removal of the calf from the dam and the associated decrease in metabolisable energy intake, any HGP response to an oestrogenic implant alone is likely to be less than that to the first combination implant. If the weaners were in a weight loss situation, the implant would be unhelpful until such time as it rained and the cattle started to gain weight again. Any HGP response would depend on good nutritional conditions occurring while the implant was still functional so the full potential benefit would be achieved from the implant. Of course, if the weaners had access to supplementary feed and weight gain was continuous, post-weaning accelerated growth would also continue.

An alternative strategy would be to delay the first implantation until just before the onset of expected seasonal rains when cattle can be assuredly mustered. This strategy would forego the additional weight gain during the suckling phase, but would not waste hormone release from an implant into a weaner that did not have the capacity to exhibit accelerated growth during periods of sub-maintenance nutrition.

For cattle in continual weight gain, regular reimplantation results in higher weight gains than one long-acting 400 day implant [28]. Whether it is economically beneficial to muster cattle just to implant was examined using costs of labour and materials as they were in 2000 [30]. An independent consultant found that for some typical regions in northern Australia it was economically attractive to muster animals just to implant if mustering costs were less than about $5 per head. A practical program might involve implantation of slaughter generation cattle whenever they are mustered for other routine husbandry procedures. This would involve having a planned schedule and matching the period of anabolic activity of the implants with the intervals between musters.

There are a number of studies [30,114] that document an attenuation of the liveweight advantage of implanted cattle relative to non-implanted controls once the influence of the implant is over. These

results suggest that once an implant program commences it should continue through to slaughter. Such a strategy does run the risk of hormone wastage during periods of liveweight loss during tough seasonal conditions. On the other hand in some parts of Australia, it is not possible to muster cattle for some time after the onset of seasonal rains. Having a long-acting implant in place "ready to go" takes immediate advantage of any increase in the animal's plane of nutrition.

One product, Progro T-S is specifically designed to be used on conjunction with long-acting oestradiol implants. It contains 140 mg trenbolone acetate and can be used to make a "combination implant" to take advantage of good nutritional conditions. Cattle with a functional silastic rubber implant can be mustered as soon as possible after the first onset of seasonal rains and treated with this product containing only trenbolone acetate. Provided there are follow-up rains, these cattle should experience a further growth boost for the next few months.

The section on body compositional changes drew attention to the fact that animals treated with an HGP have a higher mature weight than those not treated. The corollary is that at any liveweight before mature weight, treated animals are likely to be less fat than those growing without hormonal enhancement. This is especially so with the androgens, testosterone and trenbolone acetate, which actively promote leanness. Thus there are implications for markets which demand a specified degree of fatness at a specified liveweight. In general, the changes in body composition due to HGP treatment are less likely to prevent cattle breeds of early and medium maturity meeting such market specifications. Late maturing breeds which in normal circumstances might struggle to reach the specified degree of fatness might struggle even further when subjected to a whole of life HGP program.

Effects on bulls husbanded for meat production

The traditional practice of castration is intended to produce animals that are easier to manage and have a more marketable carcass. In general, castration minimises the lack of finish and tenderness problems that are often associated with bulls. It is the most common method of hormonal modification. The removal of the testes reduces the production of the males' natural anabolic steroids, testosterone and oestradiol. The low androgen and oestrogen activity of cattle compared to some other mammals and their capacity to exhibit a growth response to the provision of supplementary exogenous hormones was mentioned earlier in the section on mechanisms of action. Leaving male cattle intact lessens their reliance on externally administered hormones for the achievement of maximum growth rates.

The growth response to implantation depends on the stage of growth of the intact male. There is generally a reliable growth response to oestrogenic implants [118,119] and combinations of oestrogens and androgens [118,120] during the pre-pubertal phase of growth. The magnitude of the growth response to zeranol implants is similar to that in steers (5-23 %) [121].

From about 9 months of age and 250 plus kg liveweight, the recorded growth response of implanted bulls has been inconsistent, presumably because the animals' endogenous hormone productions are sometimes sufficient for near maximal growth rates at the pertaining nutritional conditions [122]. Some bulls implanted with oestrogenic hormones alone have exhibited increased growth rates of the order of 6-10 % [123,124] but others have exhibited minimal increases in growth rate [125,126 cited by 122,127].

Results with combination implants have been similarly inconsistent with both positive [128,129] and nil response [130,131].

From a review of the scientific literature comparing carcass compositions of bulls and steers, it was concluded that bulls have less subcutaneous fat, less marbling, less kidney fat, larger muscle areas, and lower carcass quality grades than steers [132]. Bull carcasses are more physiologically mature on the basis of bone ossification than steers of the same chronological age [133]. As

implantation of steers with growth promoting hormones advances bone ossification, it could be expected that implantation of bulls would promote ossification even further. This would have implications under the MSA grading system for bulls as the system applies a penalty for excessive ossification.

Implantation of bulls slaughtered at commercial liveweights appears to have a more consistent effect on carcass composition than on growth rates. This applies equally to implants containing oestrogenic hormones alone or a combination implant. The modification in carcass composition occurs whether or not there is a growth response to the implant. It is an essentially universal finding that implanted bulls have a fatter carcass than their non-implanted contemporaries [123, 127, 130]. More specifically, there is greater depth of subcutaneous fat [63,127] and more fat in the intermuscular depots [63]. Lifelong treatment with zeranol (5 serial implants) did not enhance marbling [123]. This association of implantation and fat deposition is the opposite effect to HGP treatment of steers. The mechanism by which this occurs appears not to be known.

The general finding is that bull meat has acceptable eating quality, though slightly below that of comparable steers [132].

Behaviour and side effects

Implanting cattle with oestrogenic and/or androgenic hormones causes minor changes to the animals' physiology which can modify their appearance, their behaviour or their social interactions with other animals. Some, like the suppression of oestrus in feedlot heifers, are desirable, but most others are unsightly to cattleman and in extreme cases can lead to economic loss. There are anecdotal reports from producers and observations from researchers that steers treated with androgenic hormones exhibit aggressive behaviour and are difficult to manage in the first months after implantation. The side effects are generally rare and have minor economic significance compared to the performance benefits realised from the use of implants [134].

Oestrus related activities in feedlot heifers can reduce the efficiency of feed conversion and impair growth [135,136]. As implantation with trenbolone acetate can suppress oestrus activity for up to 100 days [108] the full growth response to the implant can be realised [137].

The androgenic activity of trenbolone acetate is 3-5 times that of testosterone [14]. Consequently, implantation with trenbolone acetate, especially repeat implantation, leads to more accelerated development of bull-like characteristics than implantation with testosterone. The slight increase in forequarter musculature of steers and heifers implanted with trenbolone acetate was documented in the body composition section. There is anecdotal evidence from producers that steers treated with the 140 mg trenbolone acetate products exhibit more aggressive behaviour than normal for steers in the first weeks after implantation.

Cattle treated with androgens, principally trenbolone acetate, have the potential for an increased incidence of dark cutting meat [138]. Altered physiological functions, such as increased physical activity, draws heavily on glycogen stores in the muscle and leaves them depleted. If this occurs during transport or lairage, dark cutting meat post-slaughter can result. The aggressive behaviour of bulls increased the incidence of dark cutting meat [132,139,140] so any increase in aggressive behaviour of steers associated with androgen treatment is likely to have some effect, especially if steers are transported to abattoirs while the implant is still paying out appreciable amounts of hormone. Though the percentage of dark cutters was much less than one %, it was reduced further in cattle that were slaughtered more than 100 days after the last implantation [138]. Feedlot heifers given an oestrogenic implant as the final implant had a higher incidence of dark cutting than heifers given oestrogen plus trenbolone acetate as the final implant [138]. These authors stress that it is not the use of HGP products alone that increase the incidence of dark cutting, but more often the misuse, the off-label use (for example using heifer products containing a high dose of androgen in steers) and over use (double or triple implanting) that greatly increases the risk of dark cutting, increasing it to as much as 6 %.

The labels of HGP products carry the warning that vaginal, rectal and preputial prolapse, increased bulling activity, hightail, sunken loins, ventral oedema and udder development may occur as a side effect of treatment. For some of these conditions such as bulling and udder development, there is significant scientific literature. For the others, the evidence of association with HGP treatment is anecdotal from reliable industry sources. The overall incidence of all these combined seems to be less than 0.5 % of animals treated [5]. The current extent of HGP sales and the steady increase in sales over recent years suggest that the beef industry does not see these side effects as a significant problem.

The incidence of preputial prolapse, generally partial, but occasionally full, linked to HGP use, is higher than vaginal or rectal prolapse, which are rarely seen. With preputial prolapse, the muscles or tendons holding the pizzle in place appear to relax allowing the pizzle to hang out to a variable extent. Loose pizzle tropical breeds are affected more than tropical breeds with a tighter pizzle while *Bos taurus* breeds appear to be unaffected [141]. Age at first implant appears to have an influence [141]. The problem seems not to develop when calves or weaners are implanted but does occur in steers implanted for the first time as adults. Any prolapses are most likely to occur soon after implantation when there is a surge of new hormone(s) into the system of the animal.

Hightail is another condition thought to be associated with the relaxation of ligaments; in this case, the sacroiliac ligaments, allowing the sacrum to rise giving the hightail effect [142]. Though the animal looks abnormal, there are no adverse effects on carcass or meat quality [142].

Bulling or the buller steer syndrome occurs in both feedlots and at pasture. It occurs when a steer is repeatedly mounted and ridden by other steers. The incidence in US feedlots is 2.5 % [143]. Along with the type and timing of administration of growth promoting hormones, the number of steers in the group, mixing of steers from different origins, warm weather and handling procedures are also involved in the incidence of the behaviour [144,145]. The scientific literature on the role of HGPs is confusing and contradictory. Some studies report that the weak oestrogenic implant, Ralgro, is associated with less bulling [144] while others report no decreased incidence [146]. Some studies report an increased incidence with reimplantation [147], others report no increase [146,148].

Summary and conclusions

Hormonal growth promotants for cattle have been registered for use in Australia for the last 30 years. Growth rates of HGP treated cattle are increased in the range of 10-30 % and feed conversion efficiencies are improved by 5-15 %. The hormones are both oestrogenic and androgenic in the form of naturally occurring oestradiol and testosterone and the xenobiotics zeranol and trenbolone acetate. Implants are formulated to contain oestrogenic compounds alone or a combination of an oestrogen and an androgen, either testosterone or trenbolone acetate. Implants are used in both the grass-fed and feedlot sectors; the total number used in Australia in 2006/07 was 6.5 million.

Their principal use in the grass-fed industry is to increase the rate of liveweight gain and produce heavier carcasses suitable for the liveweight and age specifications for high-value markets. Their main benefit in the feedlot industry results from an increased efficiency of feed conversion and the associated reduction in feed costs per unit of liveweight gain. An economic evaluation of HGP use in Australia conducted in conjunction with this scientific review estimated that HGP usage contributed an additional $210 million to the Australian beef industry in 2006-07.

The positive effect of HGP use on the rate of liveweight gain is extremely reliable and increased gains of about 0.1 kg/d routinely occur during the period of anabolic activity of the implant. This average liveweight response may be reduced when cattle go through seasonal fluctuations in the quantity and quality of feed on offer.

The anabolic actions of growth promoting hormones, especially the androgens, result in increased protein deposition, often at the expense of fat deposition. Hormonally treated cattle attain a higher mature size and weight than their non-treated contemporaries and are only at mature body composition at this higher mature weight. Thus at any liveweight before mature body composition is attained, implanted cattle are likely to be leaner than those not treated. The difference is usually in the range of 5-8 % less fat. This has commercial implications for markets which require a certain degree of fatness at given liveweight. In later maturing genotypes where fat cover may be marginal for that particular market, implantation, especially repeat implantation, may increase lean tissue deposition to the extent that cattle fail to achieve the desired fatness. This failure to meet market specifications is more likely to occur if the terminal implant contains an androgen plus oestradiol rather than just oestradiol. On the other hand, increased weight of muscle and increased leanness is desirable for other markets. Implantation with a combination of androgen plus oestradiol in the pre-slaughter months might be commercially attractive in early maturing breeds which deposit substantial amounts of fat at low liveweights.

Over recent years, clear evidence has emerged that HGP treatments have a negative effect on meat eating quality. Because eating quality is often a subjective assessment by taste panels and is influenced by a multitude of pre- and post-slaughter factors, the HGP effect is more difficult to demonstrate scientifically than a characteristic such as liveweight gain which is measured objectively and usually on more than one occasion in an experiment. The magnitude of the effect is determined by the hormonal composition of the implant and the cumulative dose of hormones when multiple implantations are involved. Implants containing both trenbolone acetate and oestradiol appear to have a greater negative effect than implants containing only oestradiol. Repeat implantation which leads to a larger cumulative dose of hormone/s delivered over a substantial duration of an animal's growth period exacerbate the extent of the negative effect. The reduction in eating quality is most marked in non-aged meat. Ageing for 21-28 days, especially in muscles which age extensively, helps to mitigate the detrimental HGP effect.

The seasonality of pasture growth in Australia, particularly northern Australia, results in extended grow-out periods for grass-fed cattle. Accordingly, extended or whole of life implant programs have been developed to ensure sustained growth promotion. No one program is universal. Factors to be considered when designing a program include the seasonality of nutritional conditions conducive to moderate to rapid liveweight gains, the genotype of the cattle, the market for which they are being prepared and the frequency with which cattle are yarded for normal husbandry procedures. Not withstanding these variables, there are general principles which are applicable in almost all situations. They are:

- Greater responses in liveweight gain are achieved when cattle are in continual positive energy balance than when they experience periods of liveweight stasis or weight loss.
- The more frequently cattle are treated with a new implant the greater the overall response in liveweight gain.
- Once an implant program has commenced, it should be continued through until slaughter if growth response is to be maximised.
- Sustained growth promotion can be achieved through repeat implantation with oestrogenic hormones or by alternate treatment of an oestrogen and a combination implant of an oestrogen plus an androgen.
- Repeat treatment with implants containing an androgen may reduce carcass fatness, increase forequarter development and result in downgrading of carcasses at slaughter.
- Oestrogenic treatment, even repeat treatment, does not modify carcass composition *per se*. Cattle attain mature carcass composition at higher mature liveweights. They may however be leaner at intermediate liveweights
- Repeated implantation, especially when use of one or more combination implants occurs, results in a reduction in eating quality. Treatment with only one, or perhaps, two

oestrogenic implants in the final years of finishing may have a lesser negative impact on eating quality.

The labels on most of the HGP products registered for use in Australia carry the recommendation that the product should not be used in breeding females. There are sound reasons for this advice for almost without exception HGP treatment of females is not associated with peak reproductive performance. Treatment with both oestrogenic and androgenic hormones delays the onset of puberty in heifers. Androgenic hormone treatment has been associated with increased abortion rates, decreased calving rates, and decreased birth weights.

The prime reason for implanting cattle with growth promoting hormones is to increase growth rate and feed conversion efficiency. In some production situations they can also be used positively to assist in achieving the carcass composition that the market requires. There are negative influences such as reduced eating quality, especially with combination implants of an androgen plus an oestrogen, modified animal behaviour, and a low incidence of unsightly side effects. When used for the purpose for which they are registered and in cattle suitable for their use, the net economic effect on the Australian beef industry is positive. In 2006/07 approximately seven % of Australia's beef production was directly attributable to the additional carcass weight from HGP use. In that year the national herd of 28 million cattle would have had to have been 30.3 million to produce the same quantity of beef without HGP use.

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Statement of Interest

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