REPORT OF THE SCIENTIFIC COMMITTEE FOR ANIMAL NUTRITION ON THE USE OF INACTIVATED CULTURES OF SELECTED ENTEROPATHOGENIC STRAINS OF E. COLI IN FEEDINGSTUFFS FOR PIGLETS

Opinion expressed 11 March 1981

TERMS OF REFERENCE (June 1980)

The Scientific Committee for Animal Nutrition is requested to give an opinion on the following questions :

1. For what reasons can preparations of inactivated cultures of selected enteropathogenic strains of E. coli not be considered as vaccines ? If they are not vaccines, should feedingstuffs supplemented with these preparations not be considered as medicated feedingstuffs particularly because of their immunological effects ?

2. What are the effects of Intagen(x) on piglets and sows when this preparation is incorporated in the ration according to the proposed conditions of use (see Background) ? Are these effects significant in healthy farm livestock with no colibacillary infection symptoms ? Has the administration of Intagen in feedingstuffs for pregnant sows a significant influence on the effects observed in piglets ?

3. Are Intagen preparations other than the one mentioned in the dossier submitted in support of the request for its admission as an additive in feedingstuffs for piglets and sows, used for animal production ? Is Intagen used for human or veterinary therapeutic purposes ?

4. Could the use of Intagen under the proposed conditions (see Background) favour the selection of intestinal bacteria resistant to therapeutic agents used for pigs ?

5. Is this use without risk for :
   - the consumer ,
   - the people involved in livestock rearing ?
   - the environment ?

6. If Intagen satisfies the requirements for admission as an additive in feedingstuffs, what should be the administration period of the supplemented feed for piglets and sows and the maximum levels of the active principles in complete feedingstuffs ?

(x) Registered trade name

BACKGROUND

Intagen was the subject of a submission in Annex II, section F, of Council Directive 70/524/EEC, of 23 November 1970, concerning additives in feedingstuffs (1), under the following conditions of use :

Species of animal : piglets up to 10 weeks, pregnant sows.

Dose in complete feedingstuffs: 0.15 % minimum of a preparation containing from 5×10^4 to 2×10^5 hemagglutination inhibition units (HIU) per kg.

OPINION OF THE COMMITTEE

1. Intagen is a heat-treated, formalinised bacterial preparation from seven specific serotypes of E. coli, all known porcine enteropathogens; the heat treatment not only inactivates the bacteria, it also liberates the polysaccharide antigens from the cell walls. The product is incorporated in a mixture of whey powder, wheat flour and citric acid and the final product termed Intagen premix is a creamy white, free-flowing powder containing from 5×10^4 to 2×10^5 HIU/kg. Intagen, incorporated in the feed acts by stimulating the cells on the surface of the intestinal villi to produce specific IgA antibodies to the seven serotypes of E. coli used in its preparation.

   It should be noted that the intestine is equipped with a specialised surface immunity to counter the harmful effects of pathogenic bacteria. This antibody system is different from other immune systems in the body in that it can only be activated by a direct application of the antigen onto the absorptive cells covering the villi. Injectable vaccines are very inefficient in stimulating the surface immune system. A feature of the secretory immune system is that it is not long lasting unlike normal blood borne immunity in which a single course of vaccination will provide protection for a considerable period of time. Antibody production (IgA) by the secretory system persists only for as long as the stimulating antigens are present. Intagen does not have a long-term effect and must be continually administered. It acts by increasing resistance against specific pathogenic E. coli infection and thus feed containing it cannot be considered as medicated for therapeutic use.

2. Numerous trials with healthy young piglets have shown that incorporation of Intagen in the feed for an extended period of time improved weight-gain and feed conversion efficiency. In herds where E. coli infection was severe in the control piglets, its presence in the feed greatly reduced piglet mortality, increased the number of piglets weaned/litter and reduced more than half the requirement for other medication.

(1) OJ No L 270, 14.12.1970, p. 1

In sows, the continuous ingestion of Intagen with the feed from 6 weeks prefarrowing has a limited effect in increasing the immunological activity of the colostrum.

3. To achieve maximum potency of antigen activity in the colostrum of sows it is recommended that at 3 weeks before farrowing the sows, already receiving Intagen premix in their feed (see 2. above) are given a single parenteral infection of 'Intagen Injectable'. This product is a sterile preparation of the E. coli polysaccharides prepared from the heat-treated formalinised preparation referred to in 1. above. Its mode of action consists in stimulating blood borne immunity; the effect is long lasting and entirely different from that of the Intagen premix included in the feed. There is a synergistic effect between the oral and parenteral route in stimulating antigenic potency of the colostrum.

   Neither product is used for human or veterinary therapeutic purposes.

4. There is no evidence that Intagen used under the conditions proposed (see 6. below) favours the selection of intestinal bacteria resistant to therapeutic agents. Studies have shown that during Intagen administration the numbers of coliform and sulphite-reducing bacteria inhabiting the intestine are reduced while the numbers of enterococci and lactobacilli are increased. There is no evidence of increased numbers of any harmful bacteria present in the intestine after treatment has been stopped. Indeed, since the product is only specific against certain serotypes of E. coli, the intestinal flora is normal after treatment ceases. There is no adaptation of the strains of E. coli used in the preparation of Intagen to its continued use and the question of resistance developing in other E. coli strains present within the intestine does not exist by virtue of the known mode of action of the product.

5. The nature of Intagen excludes any possibility of harmful residues in animal products resulting from the feeding of it to piglets or sows. There is no risk for the consumer. Tests with guinea pigs show the absence of danger due to inhalation; the effects are much less than those caused by an egg albumin aerosol. There is no adverse effect on the environment resulting from its use, indeed the opposite may be true since its use reduces the environmental burden of toxic E. coli species.

6. The Committee considers that the conditions of use of the product should be the following :

   a) in the feed of young piglets up to 77 days of age or when the animals reach 25 kg liveweight; maximum level in complete feedingstuffs : 1 % of a preparation containing 5×10^4 to 2×10^5 HIU/kg.

   b) in the feed of sows for the period of 6 weeks prefarrowing to 3 weeks postfarrowing; maximum level in complete feedingstuffs : 0.15 % of a preparation containing 5×10^4 to 2×10^5 HIU/kg.

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