FREEDOM OF INFORMATION SUMMARY

MONENSIN + TYLOSIN IN CATTLE
FED IN CONFINEMENT FOR SLAUGHTER

I. GENERAL INFORMATION

NADA Number:	104-646
Sponsor:	Elanco Animal Health Lilly Corporate Center Indianapolis, Indiana 46285
Established Names:	Monensin sodium and tylosin phosphate
Trade Names:	Rumensin® plus Tylan® Type A Medicated Articles
Marketing Status:	Over the counter (OTC).

Effect of Supplement:

21 CFR 558.355 currently provides for the combination use of monensin and tylosin at 5 to 30 g monensin/ton of medicated feed and 8 to 10 g tylosin/ton of medicated feed to provide 50 to 360 mg monensin/head/day and 90 mg tylosin/head day in cattle fed in confinement for slaughter for improved feed efficiency and for the reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces pyogenes*.

This supplement provides for the treatment of the approved combination of monensin plus tylosin to be treated as a combination under the provisions of the Animal Drug Availability Act of 1996, and its reference to feed delivered drug combinations. The effect is to provide for the complete range (monensin, 5-30 g/ton of medicated feed to provide 50-360 mg/head/day; tylosin 8-10 g/ton of medicated feed to provide 60-90 mg/head/day) of both individually approved drugs (Type A medicated articles) in combination in Type B or C medicated feeds for cattle fed in confinement for slaughter for improved feed efficiency and for the reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces pyogenes*.

II. INDICATIONS FOR USE:

For improved feed efficiency and for the reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces pyogenes*.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE:

Dosage Form:

Both Rumensin® and Tylan® are available in 50-lb bags. Rumensin® is available as an 80 g/lb Type A medicated article and Tylan® is available as a 40 or 100 g/lb Type A medicated article.

Route of Administration:

Rumensin® and Tylan® are to be included in Type C medicated feeds for use in cattle fed in confinement for slaughter.

Recommended Dosage:

Cattle fed in confinement for slaughter should receive 5 to 30 g monensin/ton and 8 to 10 g tylosin/ton in complete feed to provide 50 to 360 mg monensin/head/day and 60 to 90 mg tylosin/head/day.

IV. EFFECTIVENESS

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act of 1996, if the active ingredients or animal drugs intended for use in combination in animal feed have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, FDA will not refuse to approve an NADA for the combination on effectiveness grounds unless the Agency finds that the NADA fails to demonstrate that 1) there is substantial evidence to demonstrate that any active ingredient or animal drug intended only for the same use as another active ingredient or animal drug in the combination makes a contribution to the labeled effectiveness, 2) each of the active ingredients or animal drugs intended for at least one use that is different from all other active ingredients or animal drugs used in the combination provides appropriate concurrent use for the intended target population, or 3) where the combination contains more than one nontopical antibacterial active ingredient or animal drug, there is substantial evidence that each of the nontopical antibacterial active ingredients or animal drugs makes a contribution to the labeled effectiveness (21 USC §512(d)(4)(D)).

Monensin as provided by Elanco, has previously been separately approved for use in cattle fed in confinement for slaughter for improved feed efficiency (21 CFR 558.355 (f)(3)(i)). Tylosin as provided by Elanco, has previously been separately approved for use in feed for beef cattle for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces pyogenes* (21 CFR 558.625 (f)(1)(i)).

Effectiveness for each drug, monensin and tylosin, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Elanco's approved NADA's 95-735 and 12-491.

Because monensin and tylosin each has at least one use that is different from all other animal drugs used in the combination, the NADA must also demonstrate that monensin plus tylosin provide appropriate concurrent use for the intended target population**.** The use of monensin plus tylosin provides appropriate concurrent use because these drugs are intended for different purposes (monensin, improved feed efficiency; tylosin, liver abscesses) likely to occur simultaneously with sufficient frequency in cattle fed in confinement for slaughter. There is no more than one nontopical antibacterial contained in this combination animal drug intended for use in Type B or C medicated feeds. Monensin is not considered to be an antibacterial animal drug for use in cattle fed in confinement for slaughter for the purposes of 512(d)(4) of the FFDCA, because monensin is classified as an ionophore.

V. ANIMAL SAFETY

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act of 1996, if the active ingredients or animal drugs intended for use in combination have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, FDA will not refuse to approve an NADA for the combination on target animal safety grounds unless there is a substantiated scientific issue specific to an active ingredient or animal drug used in the combination or a scientific issue is raised by target animal observations contained in studies submitted to the NADA for the combination and FDA finds that the application fails to establish that such combination active ingredient or animal drug is safe for the target animal.

Monensin, as provided by Elanco, has previously been separately approved for use in feed for cattle fed in confinement for slaughter for improved feed efficiency (21 CFR 558.355 (f)(3)(i)). Tylosin as provided by Elanco, has previously been separately approved for use in feed for beef cattle for reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces pyogenes* (21 CFR 558.625 (f)(1)(i)). Target animal safety for each drug, monensin and tylosin, when administered alone in accordance with its approved uses and conditions of use, is demonstrated in Elanco's approved NADA's 95-735 and 12-491. The Agency has found no substantiated scientific issue relating to the target animal safety of monensin or tylosin when used in combination under this NADA and no scientific issue has been raised by target animal observations submitted as part of the NADA for this combination. Thus, pursuant to FFDCA, as amended by the Animal Drug Availability Act of 1996, no specific target animal safety study(ies) are required for this supplemental approval of NADA 104-646.

VI. HUMAN SAFETY

In accordance with the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Animal Drug Availability Act of 1996, if the active ingredients or animal drugs intended for use in combination have previously been separately approved for the particular uses and conditions of use for which they are intended for use in combination, FDA will not refuse to approve an NADA for the combination on human safety grounds unless one or more of the active ingredients or animal drugs used in the combination at the longest withdrawal for the respective active ingredients or animal drugs in the combination exceeds the established tolerance, or one or more active ingredients or animal drugs in the combination interferes with the method of analysis for another active ingredient or drug in the combination.

Please refer to the FOI for the original approval for NADA 104-646 dated March 6, 1976 for additional human safety information concerning the use of monensin plus tylosin in cattle fed in confinement for slaughter.

VII. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA complies with the requirements of Section 512 of the FFDCA and demonstrate that monensin (5 to 30 g/ton of medicated feed to provide 50 to 360 mg/head/day) plus tylosin (8 to 10 g/ton of medicated feed to provide 60 to 90 mg/head/day) is safe and effective for improved feed efficiency and for the reduction of incidence of liver abscesses caused by *Fusobacterium necrophorum* and *Actinomyces pyogenes* in cattle fed in confinement for slaughter.

Under the Center's supplemental NADA approval policy (21 CFR 514.106(b)(2), this is a Category II change providing for the complete range (in g/ton and mg/head/day) of both individually approved drugs (Type A medicated articles) in combination in Type B or C medicated feeds. This supplement did not require a reevaluation of the safety and effectiveness data in the parent application.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for food producing animals does not qualify for marketing exclusivity because the supplemental application does not contain substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) required for the approval and conducted or sponsored by the applicant.

VIII. ATTACHED LABELING

A. Rumensin® plus Tylan® Type B Medicated Feed Bluebird Label
B. Rumensin® plus Tylan® Type C Medicated Feed Bluebird Label