

FREEDOM OF INFORMATION SUMMARY

I. GENERAL INFORMATION

A. File Number

NADA 124-309

B. Sponsor

The Upjohn Company
Agricultural Division
Kalamazoo, MI 49001

C. Proprietary Name

MGA® 100/200 Premix; MGA® 500 Liquid Premix; RUMENSIN®

D. Established Name

melengestrol acetate and monensin sodium

E. Dosage Form

Feed

F. Dispensing Status

OTC

G. Dosage Regimen

Melengestrol Acetate	0.25 to 0.4 mg/head/day
Monensin (as Monensin sodium)	50 to 360 mg/head/day (5 to 30 g/ton air dried complete feed).

NOTES:

Approval has been granted to feed 0.25 to 0.4 mg melengestrol acetate per head per day in combination with 5 to 30 g monensin per ton of air dried complete feed. Each additive may be provided via separate supplements or in a single combination supplement either liquid or dry. The supplement containing melengestrol acetate must be fed at a rate of 0.5 to 2.0 pounds per head and may be top dressed onto or mixed with a complete feed containing monensin.

H. Route of Administration

Oral

I. Indication

This supplement does not affect the labeled indications for the combination of melengestrol acetate and monensin which are:
For increased rate of weight gain, improved feed efficiency and suppression of estrus (heat) in heifers fed in confinement for slaughter.

J. Effect of Supplement

This supplement provides for removal of the requirement for a preslaughter drug withdrawal period for heifers fed melengestrol acetate in combination with monensin. Previous approvals have required a 48-hour preslaughter drug withdrawal for melengestrol acetate.

II. EFFECTIVENESS

This supplement does not affect the labeled indications for this combination.

III. ANIMAL SAFETY

The supplement does not affect target animal safety for this combination.

IV. HUMAN SAFETY

1. Tolerance and withdrawal period

As stated in the Freedom of Information Summary for the supplemental application for melengestrol acetate (NADA's 034-254 and 039-402), concurrently approved with this application, the tolerance of melengestrol acetate (MGA) is established as 25 ppb in edible tissue of treated animals and fat is designated as the target tissue for monitoring purposes. The approval also provides for the deletion of the 48-hour withdrawal period.

A tolerance of 0.05 ppm has been established for negligible residues of monensin in the edible tissues of cattle (**21 CFR 556.420**). No preslaughter withdrawal period is required for cattle fed monensin (**21 CFR 558.355**).

2. Residue depletion

Data previously summarized in Freedom of Information Summaries for NADA's 124-309 and 125-476, dated 30 April 1990, demonstrate that the concentration of melengestrol acetate in fat is below the tolerance of 25 ppb established by the approval of the supplemental application for MGA (NADA's 034-254 and 039-402) and that the concentration of monensin in liver is below its tolerance when heifers are fed melengestrol acetate, tylosin and monensin in combination; each at their highest approved dosage, and slaughtered without a pre-slaughter withdrawal. This study is summarized below.

Groups of heifers were fed for 90 days either no additive (control, n=14) or melengestrol acetate, monensin and tylosin in combination at 1X (n=7), 3X (n=7)

or 5X (n=7) the highest dosage approved for the three-way combination of these three additives (1X = 0.5 mg melengestrol acetate, 30 g monensin/ton air dried feed and 10 g tylosin/ton air dried feed). This provided melengestrol acetate at dosages of 1.25X, 3.75X and 6.25X the highest approved dosage (0.4 mg/day) for the two-way combination of melengestrol acetate and monensin. The heifers were slaughtered at practical zero withdrawal.

Perirenal fat samples were collected from all heifers for quantification of melengestrol acetate concentration using the method described in JAOAC 59:507-515:1976. This method has a limit of sensitivity of 10 ppb. All fat samples from heifers in the control and 1X treatment groups had concentrations of melengestrol acetate below 10 ppb. The average concentrations of melengestrol acetate in fat samples from heifers in the 3X and 5X dose groups were 29.2 ppb (range 18.2 to 39.6 ppb) and 42.2 ppb (range 35.8 to 49 ppb), respectively.

Liver samples were collected from seven of the control heifers and from the seven heifers in the 1X treatment group for analysis of monensin and tylosin concentration. Neither monensin or tylosin were detected in any of the liver samples. The limits of detection for these analyses were 0.04 and 0.1 ppm for monensin and tylosin, respectively.

3. Conclusion

The concentration of melengestrol acetate in fat is below the tolerance of 25 ppb and residues of monensin in liver are below the established tolerance for monensin when heifers are slaughtered without a preslaughter withdrawal following feeding of melengestrol acetate and monensin in combination at their highest approved dosage levels.

4. Assay noninterference

Data have been summarized in Freedom of Information Summaries for NADA's 124-309, 125-476, 138-792 and 138-870 demonstrating that presence of melengestrol acetate does not interfere with the tissue residue assay for monensin and presence of monensin does not interfere with the tissue residue assay for melengestrol acetate.

5. Regulatory methods

Practical regulatory methods for analysis of tissue residues of melengestrol acetate and monensin may be found in the *Food Additives Analytical Manual* on display in FDA's Freedom of Information Public Room (Parklawn Building, Room 12A30).

6. Conclusions

This supplement provides for the removal of the regulation for a 48 hour preslaughter drug withdrawal period for melengestrol acetate when melengestrol acetate and monensin are fed in combination. No changes are made in either the approved dosage range of either compound or in the target class of livestock. The data submitted support the conclusion that the concentration of melengestrol acetate in fat is below the established tolerance for melengestrol acetate and that the concentration of monensin in liver is below the established tolerance for monensin when heifers are slaughtered without a preslaughter withdrawal following the combined feeding of melengestrol acetate and monensin at their

highest approved dosage level. Accordingly, approval of this change is not expected to have adverse effects on public health or food safety.

V. AGENCY CONCLUSIONS

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change providing for the removal of the requirement for a 48 hour withdrawal period prior to slaughter for heifers fed melengestrol acetate when melengestrol acetate is fed in combination with monensin. This supplement evoked a reevaluation of the toxicity data for MGA contained in NADA's 034-254 and 039-402.

Adequate data were submitted in NADA's 034-354, 039-402, 124-309, and 125-476 which permitted the Agency to conclude that a withdrawal period is not necessary for heifers fed this combination.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval for food animals does not qualify for marketing exclusivity because the supplemental application did not contain new clinical or field investigations (other than bioequivalence or residue studies) and new human food safety studies (other than bioequivalence or residue studies) essential to the approval and conducted or sponsored by the applicant.

The format of this FOI Summary document has been modified from its original form to conform with Section 508 of the Rehabilitation Act (29 U.S.C. 794d). The content of this document has not changed.