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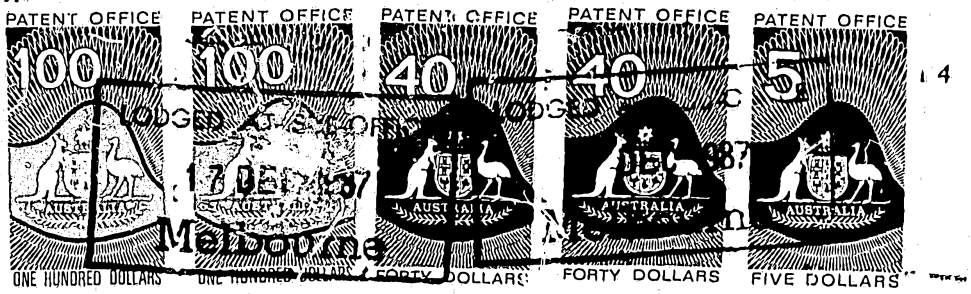

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17 DEC 1987
Melbourne

CONVENTION APPLICATION FOR A PATENT

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17 DEC 1987
Melbourne

(1) Here insert (in full) Name or Names of Applicant or Applicants, followed by Address (es).

We (1) SYNTEX (U.S.A.) INC.
of 3401 Hillview Avenue, Palo Alto, Californai 94304,
United States of America

(2) Here insert Title of Invention.

hereby apply for the grant of a Patent for an invention entitled: (2)
STABLE ANTIBIOTIC ESTER FEED COMPOSITIONS

(3) Here insert number(s) of basic application(s)

which is described in the accompanying complete specification. This application is a Convention application and is based on the application numbered (3)
944,703 and 116,421

(4) Here insert Name of basic Country or Countries, and basic date or dates

for a patent or similar protection made in (4) United States of America
on 18th December 1986 and 3rd November 1987

My/Our address for service is Messrs. Edwd. Waters & Sons, Patent Attorneys, 58 Queen Street, Melbourne, Victoria, Australia.

DATED this 16th day of December 19 87

(5) Signature (s) of Applicant (s) or Seal of Company and Signatures of its Officers as prescribed by its Articles of Association

(5) SYNTEX (U.S.A.) INC.
by
Ian A. Scott
Registered Patent Attorney

To:
THE COMMISSIONER OF PATENTS

Case 25860 Australia

(CONVENTION. ~~One or more persons.~~ Company) Form 8

COMMONWEALTH OF AUSTRALIA

Patents Act 1952-1969

DECLARATION IN SUPPORT OF A CONVENTION APPLICATION FOR A PATENT OR PATENT OF ADDITION

(1) Here insert (in full) Name or Names of Applicant or Applicants

In support of the Convention Application made by(1) SYNTEX (U.S.A.) INC.

(hereinafter referred to as the Applicant)

(2) Here insert title of Invention.

for a patent for an invention entitled:(2) STABLE ANTIBIOTIC ESTER FEED COMPOSITIONS

I/We(1) Herwig von Morze

(3) Here insert (in full) Address or Addresses

of(3) 3401 Hillview Avenue, Palo Alto, California 94304, United States of America

do solemnly and sincerely declare as follows:

1. I am/We are authorised by the applicant for the patent. to make this Declaration on its behalf.

2. The basic application s as defined by Section 141 of the Act was/were made in(4) The United States of America

(4) Here insert basic Country or Countries followed by date or dates and basic Applicant or Applicants.

on the 18 day of December 1986, by Richard A. Runkel and Stephen A. Berry

on the 03 day of November 1987, by Richard A. Runkel and Stephen A Berry

3. I am/We are the actual inventor or one of the inventors of the invention referred to in the basic application

(5) Here insert full Name(s) and Address(es) of actual Inventor(s) if other than Applicant(s).

3.(5) Richard A. Runkel, 741 Garland Drive, Palo Alto, California 94303, USA and Stephen A. Berry, 13361 Argonne Drive, Saratoga, California 95070, USA are

the actual inventors of the invention and the facts upon which I am/We are entitled to make the application, are as follow:

(6) Full Name of actual Inventor or Inventors.

I am/We are the assignee of the said(6) Richard A. Runkel and Stephen A. Berry

4. The basic application s referred to in paragraph 2 of this Declaration was/were the first application s made in a Convention country in respect of the invention the subject of the application.

DECLARED at Palo Alto, California, U.S.A.

this 20th day of November 1987

(7) Signature of Applicant or

(7) SYNTEX (U.S.A.) INC.

(12) PATENT ABRIDGMENT (11) Document No. AU-B-82650/87
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 621282

(54) Title
STABLE ANTIBIOTIC ESTER FEED COMPOSITIONS

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(21) Application No. : **82650/87** (22) Application Date : **17.12.87**

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(71) Applicant(s)
SYNTEX (U.S.A.) INC.

(72) Inventor(s)
RICHARD A. RUNKEL; STEPHEN A. BERRY

(74) Attorney or Agent
WATERMARK PATENT & TRADEMARK ATTORNEYS , Locked Bag 5, HAWTHORN VIC 3122

(56) Prior Art Documents
AU 39106/85 C07D 493/10
US 4431665
US 4394377

(57) Claim

1. An antibiotic feed premix with enhanced storage stability, which comprises:

an effective amount of an acid-sensitive antibiotic ester;

a suitable premix carrier;

an amount of veterinarily acceptable base sufficient to raise the premix pH to an antibiotic ester-stabilizing pH; and

an amount of suitable protective coating material sufficient to coat said antibiotic ester, premix carrier, and base.

17. A method for preparing animal feed premix compositions containing acid-sensitive antibiotic esters with enhanced storage stability, which method comprises:

mixing an effective amount of an acid-sensitive antibiotic ester, an amount of veterinarily acceptable base sufficient to raise the premix pH to an antibiotic ester-stabilizing pH and a suitable premix carrier to form a first mixture; and

mixing said first mixture with an amount of protective coating material sufficient to coat said antibiotic ester, premix carrier, and base to form a second mixture.

COMMONWEALTH OF AUSTRALIA 621282 Form 10

PATENTS ACT 1952-69

COMPLETE SPECIFICATION

(ORIGINAL)

Class Int. Class

Application Number:
Lodged:

Complete Specification Lodged:
Accepted:
Published:

Priority :

Related Art :

Name of Applicant : SYNTEX (U.S.A.) INC.

Address of Applicant : 3401 Hillview Avenue, Palo Alto, California 94304, United States of America

Actual Inventor: RICHARD A. RUNKEL and STEPHEN A. BERRY

Address for Service : EDWD. WATERS & SONS,
50 QUEEN STREET, MELBOURNE, AUSTRALIA, 3000.

Complete Specification for the invention entitled:

STABLE ANTIBIOTIC ESTER FEED COMPOSITIONS

The following statement is a full description of this invention, including the best method of performing it known to :- us

STABLE ANTIBIOTIC ESTER FEED COMPOSITIONS

Field of the Invention

This invention relates to a stable livestock feed premix composition containing antibiotic esters sensitive to acid in solid formulations.

This invention also relates to a method for stabilizing an acid-sensitive antibiotic ester by incorporating said ester into a feed premix composition of the invention.

Related Disclosure

Certain antibiotic esters are capable of increasing the feed efficiency of livestock, particularly ruminants. For example, laidlomycin propionate and its salts (described in U.S. Pat. No. 4,431,665, incorporated herein by reference in full) is known to increase the feed efficiency of livestock, e.g., swine, poultry, and ruminants, and also to control coccidial infections in livestock, including horses, cattle, poultry, swine, goats and sheep. Such antibiotic esters are preferably administered orally, in either the subject animal's feed or drinking water. When medicaments are to be administered to livestock orally, they are usually first

formulated in a "premix," which is then mixed into the livestock's regular feed mixture.

However, certain antibiotic esters are unstable to the acidic conditions usually present in animal feed and premixes. It has now been discovered that, for example, laidlomycin propionate and its salts are most stable in slightly acidic solutions (pH 4-6), but is most stable in solid formulations under basic conditions (pH about 11). We have now discovered that the compositions of the invention economically and effectively stabilize and protect such acid-sensitive antibiotic esters, allowing the incorporation of antibiotics such as laidlomycin esters in livestock feed without the loss of activity.

SUMMARY OF THE INVENTION

One aspect of the invention is a stable livestock feed premix which comprises an acid-sensitive antibiotic ester, a base, a protective coating, and optionally a suitable premix carrier and a sealant film.

Another aspect of the invention is a method for stabilizing acid-sensitive antibiotic esters, by granulating said esters with a base and a suitable premix carrier to form a first granulate, and coating said first granulate with a protective coating.

DETAILED DESCRIPTION AND PREFERRED EMBODIMENTS

One aspect of the invention is a stable livestock feed premix composition which comprises an acid-sensitive antibiotic ester, a base, a protective coating, optionally a suitable premix carrier, and optionally a sealant film. A preferred subgenus of the invention is the composition wherein said formulation comprises between about 0.001% to 25% antibiotic ester, about 10% to about 40% base, about 10% to about 50% protective coating, about 0% to about 50% carrier, and 0% to about

8% sealant film, especially where said acid-sensitive antibiotic ester is a laidlomycin acylate, particularly laidlomycin propionate, or its veterinarily acceptable salts. A preferred class of the invention is the composition wherein said formulation comprises between about 5 to 20% antibiotic ester, about 25% to about 40% base, about 30% to about 40% protective coating, about 0% to about 50% carrier, and about 4% to about 8% sealant film, particularly where said base is calcium hydroxide, sodium hydroxide, or potassium hydroxide. A preferred subclass of the invention is the composition wherein said protective coating is a mixture of hemicelluloses, lignins, lignosulfonates, starch or sucrose, especially a hemicellulose mixture such as Masonex®. A presently preferred embodiment of the invention is the composition which comprises about 5-20% laidlomycin propionate potassium salt, about 30-40% dry Masonex®, about 0-8% petrolatum, mineral oil, or stearyl alcohol, about 30-40% $Ca(OH)_2$, and the remainder soybean mill run.

Another aspect of the invention is a method of enhancing feed efficiency or treating coccidial infection in livestock, which method comprises: orally administering a medicated feed containing a feed premix comprising an effective amount of an acid-sensitive antibiotic ester; a suitable premix carrier; an amount of veterinarily acceptable base sufficient to raise the premix pH to an antibiotic ester-stabilizing pH; and an amount of suitable protective coating material sufficient to coat said antibiotic ester, premix carrier, and base. A preferred class of the invention is the method wherein said antibiotic ester is an acylate of laidlomycin, or a veterinarily acceptable salt thereof, especially where said premix carrier is soy bean mill run or calcium carbonate, particularly where said base is calcium hydroxide, sodium hydroxide, or potassium hydroxide. A

preferred subclass is the method wherein said protective coating is lignosulfonate, hemicellulose, starch or sucrose, particularly where said protective coating is hemicellulose. A presently preferred embodiment is the method in which the premix further comprises an amount of veterinarily acceptable sealant material sufficient to coat said antibiotic ester, premix carrier, base, and protective coating material, particularly where said sealant film is stearyl alcohol or glyceryl monostearate.

Premixes of the invention may also include optional ingredients such as tackifiers, antioxidants, vitamins, anthelmintics, preservatives, colorings, flavorings, minerals, other dietary supplements, and the like.

DEFINITIONS

The term "acid-sensitive antibiotic ester" refers to antibiotic esters and their veterinarily acceptable salts which are acid-labile in animal feed and are suitable for administration to livestock. Acid-sensitive antibiotic esters are antibiotic esters suitable for administration to livestock which are hydrolyzed under the acid conditions normally present in animal feed. Acid-sensitive antibiotic esters are generally most stable in solution at pHs of about 4 to about 10, but are more rapidly degraded at lower or higher pH. Such antibiotic esters are generally administered to ruminant livestock to increase feed efficiency, and may be administered to poultry to treat coccidiosis. Preferred antibiotic esters are laidlomycin acylates, particularly the acetate, propionate, butyrate, and phenylcarbamate. Laidlomycin acylates and their preparation and administration are described in U.S. Pat. No. 4,431,665 and U.S. Pat. No. 4,542,027, both of which are incorporated herein by reference in full. Other antibiotic esters include the esters of monensin,

lasalocid, salinomycin, narasin, lysocellin, lonomycin, ionomycin, grisorixin, nigericin, mutalomycin, noboritomycin, alborixin, lenoremycin, dianemycin, carriomycin, septamycin, etheromycin and the like.

The term "veterinarily acceptable salts" refers to non-toxic salts of an antibiotic ester with an appropriate cation suitable for oral administration to livestock, for example an alkali or alkaline earth cation. Presently preferred salts are laidlomycin propionate potassium salt, laidlomycin propionate sodium salt, laidlomycin propionate calcium salt, laidlomycin propionate cholate salt, and the like, particularly laidlomycin propionate potassium salt.

The term "veterinarily acceptable" as applied to components of the premix of the invention means that the component specified is acceptable for administration to livestock, particularly oral administration. "Veterinarily acceptable" encompasses compounds which may be employed in animals, even if not acceptable for use in humans. For example, calcium hydroxide would not be considered an acceptable carrier for pharmaceutical use, but is perfectly acceptable for use in veterinary applications.

The term "antibiotic ester-stabilizing pH" refers to a pH sufficiently high to stabilize an acid-sensitive antibiotic ester in the solid phase.

The term "effective amount" refers to the amount of antibiotic ester needed to effect the result desired. For example, the effective dosage of laidlomycin esters for increasing the feed efficiency of ruminants is generally between about 0.1 and 1.0 mg/Kg/day body weight, preferably from about 0.3 to about 0.8 mg/Kg/day. An effective dose for increasing the feed efficiency of swine is generally between about 0.1 and 10 mg/Kg/day body weight, preferably from about 1.0 to

about 5.0 mg/Kg/day. (Feed premixes for swine are preferably formulated at a laidlomycin ester concentration of about 10 to 100 mg/Kg of feed.) The effective dosage of laidlomycin esters for treating coccidial infections in livestock is generally between about 0.1 and 3.0 mg/Kg/day.

The term "base" as used herein refers to veterinarily acceptable bases which are capable of raising the pH of the premix formulation to an alkalinity at which the acid-labile antibiotic ester is stable, such as calcium hydroxide, sodium hydroxide, potassium hydroxide, sodium acetate, calcium carbonate, trisodium phosphate, triethanolamine, magnesium hydroxide, magnesium carbonate, sodium carbonate, and the like. The preferred pH of the final premix formulation is between about 8 and about 12, preferably about 9-12, most preferably about 11.

The term "livestock" as used herein refers to cattle, horses, poultry, swine, goats, sheep, and the like. It is to be appreciated that the premix of the invention is also suitable for administration to all domestic or wild animals.

The term "premix carrier" refers to edible, non-toxic compositions suitable for incorporation in livestock feed, such as calcium carbonate, soybean mill run, rice mill hulls, wheat middlings, wheat bran, corn gluten, corn gluten meal, and other mill run byproducts. Note that some suitable premix carriers may also serve as "bases" within the practice of the invention. For example, one can formulate a composition of the invention using calcium carbonate as both the premix carrier and the base.

The term "protective coating" refers to a material which, when granulated with an acid-sensitive antibiotic ester and a suitable premix carrier, is capable of

protecting said acid-sensitive antibiotic ester from the acidic conditions normally present in livestock feed. Exemplary protective coatings are hemicellulose mixtures (e.g., Masonex®), reed lignin derivatives (e.g., Glutrin®, Norilig®, and Ameribond®, available from Reed Lignin, Inc., Rothschild, Wisconsin), corn syrup solids, dextrose, starch, hydroxypropylmethylcellulose, methylcellulose, stearic acid, dextrans, cyclodextrans, or sucrose, particularly Masonex® or reed lignin. The protective coating material is generally applied to a granulate comprising the premix carrier, antibiotic ester, and base. This may be accomplished by adding a slurry of protective coating material to the first granulate, or by mixing the first granulate with the protective coating material as a dry powder.

The term "sealant film" refers to an optional coating which may be applied to the granulated antibiotic ester-protective coating composition to provide further protection against acidic conditions. Exemplary sealant film materials are stearyl alcohol, glyceryl monostearate, sodium oleate, stearic acid, glyceryl monostearate, sodium caseinate, sorbitol, paraffin wax, petrolatum, mineral oil, gelatin, and the like. Sealant films are applied to the composition after the protective coating has been applied (e.g., the second granulate). The sealant film may be applied by dissolving the sealant film material in a volatile solvent (e.g., methanol), spraying the resulting solution over the second granulate, and drying the resulting composition to remove the volatile solvent. Alternatively, one can add the sealant film material to the second granulate as a solid, and gently heat the mixture to melt the sealant film material. The latter method is suitable for use with low-melting materials, e.g., materials which melt at

temperatures of 60°C or less, in order to avoid degrading the antibiotic ester.

The term "Masonex®" refers to a hemicellulose extract by-product of Masonite board process. Masonex® is a viscous, dark-colored syrup which is commonly about 50% mixed hemicelluloses and 50% water. Masonex® is commercially available from Masonite Corporation.

PREPARATION

Compositions of the invention are prepared by the following procedures:

The antibiotic ester is first dispersed in an aqueous slurry of base. The resulting dispersion is then used to granulate the premix carrier. The resulting moist granulate is then air dried, followed by further granulation with a slurry of protective coating material. This second granulate is also dried, e.g., using warm air. If desired, one may apply a sealant film to this dried second granulate either by adding a methanol solution of the sealant while stirring the dried second granulate, or by simply mixing in solid sealant and applying enough heat to melt the sealant. The resulting sealed or unsealed second granulate can be mixed with animal feed at the appropriate concentration to produce an animal feed premix formulation suitable for administration to livestock.

Alternatively, one may granulate the premix carrier with a slurry of aqueous base. The resulting moist granulate is then air dried, followed by further granulation with a slurry of antibiotic ester mixed with the protective coating material. This second granulate is also dried, e.g., using warm air. If desired, one may apply a sealant film to this dried second granulate either by adding a methanol solution of the sealant while stirring the dried second granulate, or by simply mixing

in solid sealant and applying enough heat to melt the sealant. The resulting sealed or unsealed second granulate can be mixed with animal feed at the appropriate concentration to produce an animal feed premix formulation suitable for administration to livestock.

One may also prepare the premix of the invention by fluid bed granulation. This is presently the preferred method of manufacture. For example, the antibiotic ester, carrier and base are mixed together and spread in a fluid bed reactor. The powder mixture is fluidized with air at about 80°C, and granulated with Masonex® (the Masonex® is diluted with water until an appropriate viscosity is obtained.) The mixture is granulated and dried in the fluid bed reactor for a total time of about 1-3 hours, at a bed temperature of about 20-40°C.

The finished formulation should contain between about 0.001% and 25% antibiotic ester, 10% to about 40% base, about 10% to about 50% protective coating, about 0% to about 50% carrier, and 0% to about 8% sealant film. In formulations containing little or no carrier, the base is used in a granulated form and also plays the role of carrier.

Compositions of the invention may be prepared by other methods as well. A suitable method will produce a particulate premix composition wherein a suitable premix carrier mixed with an acid-sensitive antibiotic ester and a suitable base form the cores of the premix particles. These cores are coated in a layer of protective coating material, and optionally coated with an additional sealant film.

The following examples are presented for the purposes of illustration, and are not intended to limit the scope of the invention in any way.

EXAMPLE 1

(Formulations)

The following are exemplary formulations of the invention:

(A) Premix 1:

Ingredient	Amount
Laidlomycin propionate, K+	10.0 Kg
$Ca(OH)_2$	20.0 Kg
Masonex® (pH adjusted to 12)	30.0 Kg (solid wt)
$CaCO_3$	10.0 Kg
Soybean mill run q.s.	100.0 Kg

The laidlomycin propionate potassium salt is dispersed in an aqueous slurry of $Ca(OH)_2$. The resulting dispersion is then used to granulate the $CaCO_3$. The resulting moist granulate is then air dried, followed by further granulation with a slurry of Masonex®. This second granulate is also dried using warm air to form a premix composition of the invention.

This premix is then mixed with Gali® Chick Mash in a ratio of 1:1,000 to form a finished feed suitable for administration to livestock, particularly chickens, turkeys, and ducks.

(B) Premix 2:

Ingredient	Amount
Laidlomycin propionate, K+	5.0 g
$Ca(OH)_2$	9.0 g
Masonex® (pH adjusted to 12)	10.0 g (solid wt)
Stearyl alcohol	5.0 g
Soybean mill run q.s.	50.0 g

The soybean mill run is first granulated with a slurry of aqueous $Ca(OH)_2$. The resulting moist granulate is then air dried, followed by further granulation with a slurry of laidlomycin propionate potassium salt and Masonex®. This second granulate is

also dried using warm air. Next, a sealant film is applied to this dried second granulate by adding a methanol solution stearyl alcohol while stirring the dried second granulate, then drying with warm air to remove the methanol.

The resulting sealed second granulate is mixed with animal feed at a ratio of about 1:1,000 to produce an animal feed premix formulation suitable for administration to livestock.

(C) Fluid Bed Premix:

Ingredient	Amount
Laidlomycin propionate, Na+	595.2 g
$Ca(OH)_2$	1800.0 g
Masonex• (pH adjusted to 12)	2400.0 g (solid wt)
Petrolatum	240.0 g
Soybean mill run	964.8 g

The laidlomycin propionate sodium salt, $Ca(OH)_2$, and soybean mill run are weighed and mixed in a fluid bed unit for 5-10 minutes. The Masonex• solution is adjusted to pH 12 using NaOH, and is sprayed into the unit to granulate the dry mixture. The resulting granulate is then dried in the unit until the moisture is reduced to about 5-6%. Then, the petrolatum (or optionally mineral oil #35) is melted by heating to 70-75°C, and sprayed on the dried granulate. (Petrolatum or mineral oil serves as a tackifier to prevent settling of the premix in the final feed formulation.) The tackifier may alternatively be added in a planetary mixer. The premix thus prepared is approximately the same density as animal feed, and so resists settling and segregation.

The resulting premix is mixed with animal feed at a ratio of about 1:1,000 to produce an animal feed premix formulation suitable for administration to livestock,

particularly cattle. Alternatively, the premix may be diluted about 1:500 to produce an animal feed premix formulation suitable for administration to livestock such as swine.

EXAMPLE 2

(Stability Study)

Test compositions were prepared as follows:

Ingredient	Concentration		
Composition:	A	B	C
Laidlomycin Propionate K+	10%	10%	10%
$CaCO_3$	30%	30%	20%
50% Masonex• (pH 10)	0%	30%	0%
Stearic acid	0%	0%	10%
Soybean mill run	qs	qs	qs

Composition A was prepared by first mixing the soybean mill run with an aqueous slurry of $CaCO_3$, then an aqueous slurry of laidlomycin propionate potassium salt. The resulting composition was granulated and air-dried.

Composition B was prepared by first mixing the soybean mill run with an aqueous slurry of $CaCO_3$. The laidlomycin propionate K+ was then dispersed in the Masonex• and the dispersion extended into the soybean mill run/$CaCO_3$ blend. The resulting mixture was dried to 11% moisture.

Composition C was prepared by dispersing $CaCO_3$ a. laidlomycin propionate K+ in liquid stearic acid (50-55°C). The dispersion was allowed to congeal, milled, and mixed with soybean mill run.

Each of these compositions was then blended with chicken feed at a ratio of 1:1,000, and sealed in glass bottles. The bottles were stored at 40°C for three months, opened, and the percentage laidlomycin propionate

potassium salt (LP) remaining was determined. The results are set out in Table I.

TABLE I.

Composition	Percent LP (+/- SD) initial	final
A	97.0±2.6	32.0±1.7
B	91.0±6.2	60.0±2.8
C	108.0±6.7	32.0±4.0

These results indicate that the compositions of the invention significantly increase the stability of pH-sensitive antibiotic esters.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:
~~WHAT IS CLAIMED~~:

1. An antibiotic feed premix with enhanced storage stability, which comprises:

an effective amount of an acid-sensitive antibiotic ester;

a suitable premix carrier;

an amount of veterinarily acceptable base sufficient to raise the premix pH to an antibiotic ester-stabilizing pH; and

an amount of suitable protective coating material sufficient to coat said antibiotic ester, premix carrier, and base.

2. The premix composition of Claim 1 wherein said antibiotic ester is an acylate of laidlomycin, or a veterinarily acceptable salt thereof.

3. The premix composition of Claim 2 wherein said premix carrier is soy bean mill run or calcium carbonate.

4. The premix composition of Claim 3 wherein said base is calcium hydroxide, sodium hydroxide, or potassium hydroxide.

5. The premix composition of Claim 4 wherein said protective coating is lignosulfonate, hemicellulose, starch or sucrose.

6. The premix composition of Claim 5 wherein said protective coating is hemicellulose.

7. The premix composition of Claim 1 which further comprises an amount of veterinarily acceptable sealant material sufficient to coat said antibiotic

ester, premix carrier, base, and protective coating material.

8. The premix composition of Claim 7 wherein said sealant film is stearyl alcohol or glyceryl monostearate.

9. An animal feed premix composition with enhanced storage stability for treating coccidiosis or increasing feed efficiency, which composition comprises:

0.001% to 25% acid-sensitive antibiotic ester;

10% to about 40% veterinarily acceptable base;

10% to about 50% suitable protective coating material;

0% to about 50% suitable premix carrier; and

0% to about 8% veterinarily acceptable sealant film material.

10. The composition of Claim 9 wherein said acid-sensitive antibiotic ester is a laidlomycin acylate, or a veterinarily acceptable salt thereof.

11. The composition of Claim 10 wherein said laidlomycin acylate is an alkali metal or alkaline earth salt of laidlomycin propionate.

12. The composition of Claim 11 wherein said composition comprises:

5 to 20% laidlomycin propionate salt;

25% to 40% base;

30% to 40% protective coating;

0% to about 50% carrier; and

4% to 8% sealant film.

13. The composition of Claim 12 wherein said base is calcium hydroxide, sodium hydroxide, or potassium hydroxide.

14. The composition of Claim 12 wherein said protective coating is hemicellulose, starch or sucrose.

15. The composition of Claim 14 wherein said protective coating is hemicellulose.

16. The composition of Claim 15 wherein said composition comprises:

5-20% laidlomycin propionate potassium salt;
30-40% hemicellulose (dry weight);
0-8% stearyl alcohol;
30-40% $Ca(OH)_2$; and
soybean mill run to produce 100%.

17. A method for preparing animal feed premix compositions containing acid-sensitive antibiotic esters with enhanced storage stability, which method comprises:

mixing an effective amount of an acid-sensitive antibiotic ester, an amount of veterinarily acceptable base sufficient to raise the premix pH to an antibiotic ester-stabilizing pH and a suitable premix carrier to form a first mixture; and

mixing said first mixture with an amount of protective coating material sufficient to coat said antibiotic ester, premix carrier, and base to form a second mixture.

18. The method of Claim 17 wherein said acid-sensitive antibiotic ester is laidlomycin propionate or a veterinarily acceptable salt thereof.

19. The method of Claim 18 wherein said premix carrier is soy bean mill run or calcium carbonate.

20. The method of Claim 19 wherein said base is calcium hydroxide, sodium hydroxide, or potassium hydroxide.

21. The method of Claim 20 wherein said protective coating is hemicellulose, starch or sucrose.

22. The method of Claim 20 wherein said protective coating is hemicellulose.

23. The method of Claim 17 which further comprises: coating said second mixture with a sealant film.

24. The method of Claim 23 wherein said sealant film is petrolatum, mineral oil, stearyl alcohol or glyceryl monostearate.

25. A method of enhancing feed efficiency or treating coccidial infection in livestock, which method comprises:

orally administering a medicated feed containing a feed premix comprising

an effective amount of an acid-sensitive antibiotic ester;

a suitable premix carrier;

an amount of veterinarily acceptable base sufficient to raise the premix pH to an antibiotic ester-stabilizing pH; and

an amount of suitable protective coating material sufficient to coat said antibiotic ester, premix carrier, and base.

26. The method of Claim 25 wherein said antibiotic ester is an acylate of laidlomycin, or a veterinarily acceptable salt thereof.

27. The method of Claim 26 wherein said premix carrier is soy bean mill run or calcium carbonate.

28. The method of Claim 27 wherein said base is calcium hydroxide, sodium hydroxide, or potassium hydroxide.

29. The method of Claim 28 wherein said protective coating is lignosulfonate, hemicellulose, starch or sucrose.

30. The method of Claim 29 wherein said protective coating is hemicellulose.

31. The method of Claim 30 which further comprises an amount of veterinarily acceptable sealant material sufficient to coat said antibiotic ester, premix carrier, base, and protective coating material.

32. The method of Claim 31 wherein said sealant film is stearyl alcohol or glyceryl monostearate.

DATED this 16th day of December 1987.

SYNTEX (U.S.A.) INC.

EDWD. WATERS & SONS
PATENT ATTORNEYS
50 QUEEN STREET
MELBOURNE. VIC. 3000.