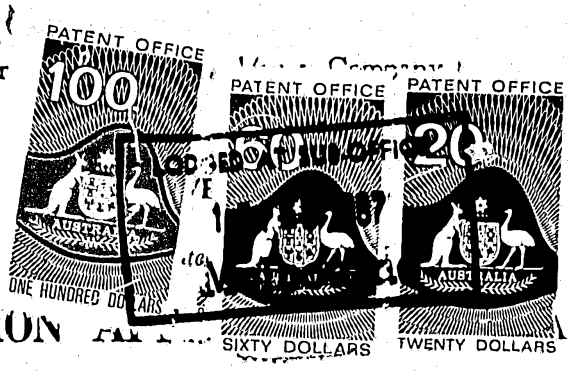
(CONVENTION. By one or ... Company ...

Form 4



CONVENTION ... PATENT

LODGED AT SUB-OFFICE
17 FEB 1987
Melbourne

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

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

FEE STAMP TO VALUE OF $ 1.80 ATTACHED
MAIL OFFICER

(2) Here insert Title of Invention.

hereby apply for the grant of a Patent for an invention entitled: (2)
ANTI-INFECTIVE INJECTABLE FORMULATIONS

(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)
830,389

(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 February, 1986.

APPLICATION ACCEPTED AND AMENDMENTS ALLOWED 22-1-90

My/Our address for service is Messrs. Edwd. Waters & Sons, Patent Attorneys, 50 Queen Street, Melbourne, Victoria, Australia.

DATED this 16th day of February, 1987

(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: [signature]

W.F. DANCER
Registered Patent Attorney.

To:

Case 25400

(CONVENTION. Company.) Form 5

COMMONWEALTH OF AUSTRALIA

Patents Act 1952-1960

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

In support of the Convention Application made by[1] Syntex (U.S.A.) Inc.

(hereinafter referred to as the applicant) for a Patent for an invention entitled:[2] Anti-Infective Injectable Formulations

I,[3] Herwig von Horze of 3401 Hillview Avenue, Palo Alto, California 94304, U.S.A.

do solemnly and sincerely declare as follows:

1. I am authorised by the applicant for the patent to make this declaration on its behalf.

2. The basic application as defined by Section 141 of the Act was made in[4] United States of America on the 18 day of February 1986, by Richard C. Herschler

~~on the day of 19 by~~

3.[5] Richard C. Herschler, 1248 Stanwirth Court, Los Altos, California 94022, U.S.A.

is/~~are~~ the actual inventor of the invention and the facts upon which the applicant is entitled to make the application are as follow:

The applicant is the assignee of Richard C. Herschler

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

DECLARED at Palo Alto, California this 6th day of January 1987

SYNTEX (U.S.A.) INC.

(1) Here insert (in full) Name of Company.

(2) Here insert title of Invention.

(3) Here insert full Name and Address, of Company official authorized to make declaration.

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

(5) Here insert (in full) Name and Address of Actual Inventor or Inventors.

(12) PATENT ABRIDGMENT (11) Document No. AU-B-68876/87
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 595287

(54) Title
INJECTABLE COMPOSITION OF AN ANTIBIOTIC AND ANOTHER ACTIVE COMPONENT

International Patent Classification(s)
(51)[4] A61K 009/08 A61K 031/65 A61K 031/557

(21) Application No. : 68876/87 (22) Application Date : 17.02.87

(30) Priority Data

(31) Number (32) Date (33) Country
830389 18.02.86 US UNITED STATES OF AMERICA

(43) Publication Date : 20.08.87

(44) Publication Date of Accepted Application : 29.03.90

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

(72) Inventor(s)
RICHARD C. HERSCHLER

(74) Attorney or Agent
WATERMARK MELBOURNE

(57) Claim

2. A composition suitable for parenteral injection for inducing estrus in a female mammal, or abortion or parturition in a pregnant mammal, which composition comprises:

an effective amount of a $PGF_{2}\alpha$ derivative;

a systemically sub-therapeutic amount of an antibiotic; and

a pharmaceutically acceptable carrier.

Form 10

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952-69

COMPLETE SPECIFICATION

(ORIGINAL)

Class Int. Class

Application Number:
Lodged: 68876/87

595287

Complete Specification Lodged:
Accepted:
Published:

Priority :

Related Art :

This document contains the amendments made under Section 49.

and is correct for printing.

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 C. HERSCHLER

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

Complete Specification for the invention entitled:

ANTI-INFECTIVE INJECTABLE FORUMLATIONS

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

ANTI-INFECTIVE INJECTABLE FORMULATIONS

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to methods for preventing infection associated with subcutaneous or intramuscular injection of mammals with parenteral formulations, especially prostaglandin formulations, and new compositions containing parenterally administrated compounds with a systemically sub-therapeutic amount of an antibiotic.

Related Disclosure

It is frequently desirable to administer compounds to livestock by parenteral injection. For example, vaccines, hormones, vitamins and nutritional supplements are frequently administered by intramuscular injection.

$PGF_2\alpha$ and certain $PGF_2\alpha$ derivatives are useful for controlling the reproductive cycles of female mammals. For example, methyl (±)-9α,11α,15α-trihydroxy-16-phenoxy-17,18,19,20-tetranorprosta-4,5,13-(E)-trienoate (known generically as fenprostalene) is used to induce estrus, abortion, or parturition in female mammals, particularly horses, cattle, and swine. Fenprostalene is described in U.S. Pat. No. 3,985,791,

which is incorporated herein by reference in its entirety. Other known $PGF_2\alpha$-type compounds include Cloprostenol, Dinoprost, Luprostiol, Alfaprostol and the like. $PGF_2\alpha$ and its derivatives are most commonly administered via subcutaneous or intramuscular injection.

However, due to the conditions under which livestock are usually injected, this method of administration carries some risk of infection. Administration is most commonly performed in areas which are far from aseptic, and parenteral injection can carry normally harmless bacteria through the hide where it may cause serious infection.

It has now been discovered that one may prevent such infection by incorporating a small amount of an antibiotic in the injection formulation. Surprisingly, the amount of antibiotic required is far less than the usual systemic dosage.

DEFINITIONS

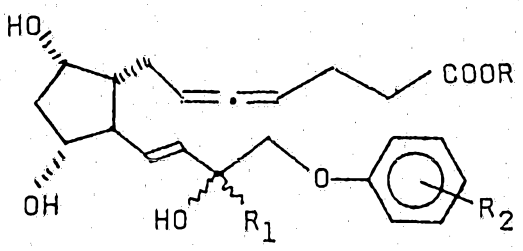
The term "antibiotic" as used herein includes all commonly used bacteristatic and bactericidal antibiotics, which are suitable for parenteral injection. Antibiotics include aminoglycosides, such as amikacin, gentamicin, kanamycin, neomycin, streptomycin, and tobramycin; cephalosporins, such as cefamandole, cefazolin, cephalexin, cephaloglycin, cephaloridine, cephalothin, cephapirin, and cephradine; macrolides, such as erythromycin and troleandomycin; penicillins, such as penicillin G, amoxicillin, ampicillin, carbenicillin, cloxacillin, dicloxacillin, methicillin, nafcillin, oxacillin, phenethicillin, and ticarcillin; polypeptide antibiotics, such as bacitracin, colistimethate, colistin, polymyxin B; tetracyclines, such as chlortetracycline, demeclocycline, doxycycline, methacycline, minocycline, tetracycline, and

oxytetracycline; and miscellaneous antibiotics such as chloramphenicol, clindamycin, cycloserine, lincomycin, rifampin, spectinomycin, vancomycin, and viomycin. Additional antibiotics are described in "Remington's Pharmaceutical Sciences," 16th Ed., (Mack Pub. Co., 1980), pp. 1121-1178. Presently preferred antibiotics are penicillin, tetracycline, and oxytetracycline, particularly oxytetracycline. Recommended daily systemic doses of oxytetracycline for intramuscular injection in animals range from about 6.5 mg/Kg to about 20 mg/Kg.

The term "parenterally suitable compound" refers to compounds which are commonly administered by subcutaneous or intramuscular injection. Parenterally suitable compounds include, without limitation, vaccines, hormones, vitamins, nutritional supplements, and the like. Preferred parenterally suitable compounds are steroid hormones and prostaglandin derivatives, especially $PGF_2\alpha$ and its derivatives.

The term "$PGF_2\alpha$ derivative" refers to prostaglandin $F_2\alpha$ and prostaglandin derivatives with activity similar to prostaglandin $F_2\alpha$ (also known as dinoprost tromethamine). Presently preferred $PGF_2\alpha$ derivatives are compounds of formula 1:

(1)



or a pharmaceutically acceptable salt thereof, wherein

R is hydrogen or lower alkyl;

R_1 is hydrogen, methyl, or ethyl;

R_2 is hydrogen, halo, trifluoromethyl, lower alkyl or lower alkoxy.

The term "lower alkyl" refers to straight or branched saturated monovalent hydrocarbon radicals containing four carbon atoms or less, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, s-butyl, i-butyl, and t-butyl.

The term "lower alkoxy" refers to radicals of the form RO-, where R is lower alkyl as defined above.

The term "halo" refers to the halogen radicals fluoro, chloro, bromo, or iodo.

The term "effective amount" as used herein refers to the amount of $PGF_2\alpha$ derivative needed to effect induction of estrus, abortion, or parturition in a female mammal. As $PGF_2\alpha$ derivatives are known and used in the art, the effective amount of any particular $PGF_2\alpha$ derivative will be known or readily determined by the practitioner of ordinary skill. In general terms, an effective amount of fenprostalene for induction of parturition, for induction of estrus, or for induction of abortion is from about 0.0022 mg/Kg to about 0.011 mg/Kg, preferably from about 0.0022 mg/Kg to about 0.0044 mg/Kg, and most preferably about 0.0033 mg/Kg. The exact dosage may vary with the species of mammal and the condition being treated. However, such variations are readily predicted by one of ordinary skill.

The term "systemically sub-therapeutic dose" refers to the amount of antibiotic needed to prevent infection associated with intramuscular injection. A systemically sub-therapeutic dose is less than the usual dose prescribed for systemic treatment of infection. For example, oxytetracycline is normally prescribed for mammals in doses of about 11 mg/Kg per day (i.m.), whereas the dosage administered in the practice of the invention can be less than about 0.20 mg/Kg per

injection. A systemically sub-therapeutic amount of oxytetracycline for prevention of infection associated with intramuscular injection ranges from about 0.018 mg/Kg to about 0.14 mg/Kg, preferably from about 0.035 mg/Kg to about 0.14 mg/Kg, and most preferably about 0.10 mg/Kg. In any case, a systemically sub-therapeutic amount is less than 1.0 mg/Kg.

The term "pharmaceutically acceptable acid addition salts" refers to salts of the subject compounds which possess the desired pharmacological activity and which are neither biologically nor otherwise undesirable. These salts are formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid or phosphoric acid; or organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, malonic acid, succinic acid, malic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid and the like.

The term "mammal" as used herein refers to domesticated mammals such as cattle, horses, swine, sheep, goats, dogs, cats, and the like.

All percentages used herein are "weight/weight" percentages (w/w).

The term "parenteral injection" as used herein refers to administration by subcutaneous or intramuscular injection.

SUMMARY OF THE INVENTION

One aspect of the invention is a composition suitable for parenteral injection for inducing estrus in a female bird or mammal, or abortion or parturition in a pregnant mammal, which composition comprises an effective amount of a $PGF_{2\alpha}$ derivative, a systemically sub-therapeutic

The present invention therefore provides a composition suitable for parenteral injection in a bird or mammal, which composition comprises :

an effective amount of a parenterally suitable compound;

a systemically sub-therapeutic amount of an antibiotic; and

a pharmaceutically acceptable carrier. The present invention also provides a composition suitable for parenteral injection for inducing estrus in a female mammal, or abortion or parturition in a pregnant mammal, which composition comprises :

an effective amount of a $PGF_2\alpha$ derivative;

a systemically sub-therapeutic amount of an antibiotic; and

a pharmaceutically acceptable carrier. Preferably the $PGF_2\alpha$ derivative is fenprostalene and the antibiotic is oxytetracycline. Preferably the fenprostalene is present in an amount between 0.25 mg/mL and 1.0 mg/mL and the oxytetracycline is present in an amount between 0.4% and 1.6%. Preferably the composition comprises:

0.025% - 0.050% fenprostalene;

0.4% - 1.6% oxytetracycline; and

a pharmaceutically acceptable carrier. More preferred is a composition which comprises:

0.025% - 0.050% fenprostalene;

0.025% - 0.050% dl-α-tocopherol;

0.4% - 1.6% oxytetracycline; and

a pharmaceutically acceptable carrier.

The present invention also provides a method for inducing estrus, abortion, or parturition in a female mammal without initiating infection, which method comprises :

administering a composition containing an effective amount of a $PGF_2\alpha$ derivative; a systemically sub-therapeutic amount of an antibiotic; and a pharmaceutically acceptable carrier. Preferably the $PGF_2\alpha$ derivative is fenprostalene and the antibiotic is oxytetracycline. Preferably the fenprostalene is present in an amount between 0.25 mg/mL and 1.0 mg/mL and the oxytetracycline is present in an amount between 0.4% and 1.6%. Preferably the method comprises administering a composition which comprises :

0.025% - 0.050% fenprostalene;

0.4% - 1.6% oxytetracycline; and

a pharmaceutically acceptable carrier and more preferably the composition comprises :

0.025% - 0.050% fenprostalene;

0.025% - 0.050% dl-α-tocopherol;

0.4% - 1.6% oxytetracycline; and

a pharmaceutically acceptable carrier. The invention also provides a method for administering a parenterally suitable compound to a bird or mammal without initiating infection, which method comprises:

administering a composition containing an effective amount of a parenterally suitable compound; a systemically sub-therapeutic amount of an antibiotic; and a pharmaceutically acceptable carrier. Preferably the parenterally suitable compound is a vaccine, hormone, vitamin, or nutritional supplement.

~~amount of an antibiotic, and a pharmaceutically~~ acceptable carrier.

Another aspect of the invention is the method for inducing estrus, abortion, or parturition in a female bird or mammal, which method comprises administering a composition comprising an effective amount of a $PGF_{2}\alpha$ derivative, a systemically sub-therapeutic amount of an antibiotic, and a pharmaceutically acceptable carrier.

Another aspect of the invention is the method of administering a parenterally administerable compound without while preventing simultaneous infection, by including in the parenterally administered formulation a ~~systemically sub-therapeutic amount of an antibiotic.~~

DETAILED DESCRIPTION AND PREFERRED EMBODIMENTS

One aspect of the invention is a composition for parenteral administration to a bird or mammal, which comprises a parenterally suitable compound, a systemically sub-therapeutic amount of an antibiotic, and a pharmaceutically acceptable carrier, especially where said parenterally suitable compound is a vaccine, a hormone, a vitamin, or nutritional supplement, particularly a prostaglandin or prostacyclin, or a derivative or analog thereof. A preferred sub-genus of the invention is a composition suitable for intramuscular administration to a female bird or mammal, which composition comprises an effective amount of a $PGF_{2}\alpha$ derivative, a systemically sub-therapeutic amount of an antibiotic, and a pharmaceutically acceptable carrier, especially where said $PGF_{2}\alpha$ derivative is fenprostalene and said antibiotic is oxytetracycline. A preferred class of the invention is the composition wherein said fenprostalene is present in an amount between about 0.25 mg/mL and about 1.0 mg/mL, preferably about 0.5 mg/mL. A preferred sub-class of the invention is the composition in which

said oxytetracycline is present in an amount between about 0.4% and about 1.6%, preferably about 1.6%. A presently preferred embodiment of the invention is the composition comprising

fenprostalene	0.025% -	0.1%
oxytetracycline	0.4% -	1.6%
dl-α-tocopherol	0.025% -	0.050%
PEG 400 qs		100.0%.

Another aspect of the invention is a method for administering parenterally suitable compounds without injection-associated infection, which method comprises administering a composition comprising a parenterally suitable compound, a systemically sub-therapeutic amount of an antibiotic, and a pharmaceutically acceptable carrier. A preferred sub-genus of the invention is the method wherein said parenterally suitable compound is a vaccine, hormone, vitamin or nutritional supplement.

Another aspect of the invention is the method for inducing estrus, abortion, or parturition in a female mammal without initiating infection, which method comprises administering an effective amount of a $PGF_2\alpha$ derivative, a systemically sub-therapeutic amount of an antibiotic, and a pharmaceutically acceptable carrier, especially where said $PGF_2\alpha$ derivative is fenprostalene and said antibiotic is oxytetracycline. A preferred subgenus of the invention is the method wherein said fenprostalene is present in an amount between about 0.025% and about 0.050%, preferably about 0.050%. A preferred class of the invention is the method in which said oxytetracycline is present in an amount between about 0.4% and about 1.6%, preferably about 1.6%.

The systemically sub-therapeutic amount of antibiotic necessary to prevent injection-associated

infection may be determined by one of ordinary skill by routine experimentation. For example, one may inject guinea pigs with a composition containing a test amount of antibiotic and a lethal dose of bacteria to determine the amount of antibiotic necessary. The dose of bacteria used may be a combination of several strains, or may be a representative strain such as Clostridium chauveoi. The amount of antibiotic required will be independent of the species of subject mammal, but may be dependent on the species of bacteria. Thus, experiments with small laboratory animals are sufficient to establish dosages for larger animals. The use of a large excess (e.g., 10 times the lethal dose when administered without an antibiotic) of lethal bacteria is sufficient to compensate for any variation due to differences in bacterial species.

ADMINISTRATION AND FORMULATION

One aspect of the present invention relates to pharmaceutical compositions useful for inducing estrus or parturition in female birds or mammals, comprising an effective amount of a compound of $PGF_2\alpha$ derivative and a sub-therapeutic amount of an antibiotic, in admixture with a pharmaceutically acceptable non-toxic carrier. An effective amount of a $PGF_2\alpha$ derivative is that amount which is necessary to induce estrus in a female mammal, or the amount necessary to induce parturition in a pregnant bird or mammal near the end of that bird or mammal's gestation period.

Useful pharmaceutical carriers for the preparation of the pharmaceutical compositions hereof are liquids and can take the form of solutions, suspensions, elixirs, and the like. Carriers can be selected from the various oils, including those of petroleum, animal, vegetable or synthetic origin, for example, peanut oil, soybean oil,

mineral oil, sesame oil, and the like. Water, saline, aqueous dextrose, and glycols are preferred liquid carriers. Other suitable pharmaceutical carriers and their formulations are described in "Remington's Pharmaceutical Sciences" by E. W. Martin.

The compositions of the invention are prepared in solution form using standard techniques. $PGF_{2\alpha}$ derivatives are available from commercial sources, or may be prepared by the methods taught in the art. It is preferred to include a small amount of an anti-oxidizing agent such as dl-α-tocopherol in the formulation to protect the prostaglandin from oxidation. Antibiotics are also available from commercial sources.

The compositions of the invention may be assayed for efficacy by injecting suitable test animals with mixtures of compositions of the invention and lethal doses of infectious bacteria of a type commonly found on animal hide. For example, Clostridium chauveoi is a potentially lethal species of bacteria which may be used as a suitable challenge bacteria.

EXAMPLE 1

(Formulations)

A formulation suitable for subcutaneous injection for inducing abortion, parturition, or estrus in cattle is prepared as follows:

fenprostalene		0.5 mg
oxytetracycline		16.0 mg
dl-α-tocopherol		0.5 mg
sterile polyethylene glycol 400	qs	1.0 mL

The fenprostalene and oxytetracycline are added to a solution of dl-α-tocopherol and sterile polyethylene glycol 400, and the resulting solution is mixed well.

EXAMPLE 2

(Formulations)

Other formulations suitable for intramuscular injection in cattle were prepared as follows:

(A) Progesterone

progesterone		100.0 mg
oxytetracycline		16.0 mg
sterile water for injection	qs	5.0 mL

(B) Oxytocin

purified oxytocin principle (10 U/mL)	1.5 mL
oxytetracycline	16.0 mg
sterile water for injection	1.0 mL

(C) Cortisone acetate:

cortisone acetate		1.5 g
oxytetracycline		16.0 mg
sterile water for injection	qs	5.0 mL

EXAMPLE 3

(Guinea Pig Assay)

Nine groups of five Guinea pigs (587-720 g/animal, Biolabs) were selected at random for challenge with *Clostridium chauveoi*. A 0.5 mL (100 LD_{50} per 0.5 mL dose) dose of the indicated formulation (containing PEG 400, dl-α-tocopherol, oxytetracycline, and *C. chauveoi*) was administered by intramuscular injection to the left rear leg of each animal:

Group#	Formulation			
	C. chauveoi (per mL)	PEG 400 (for 1 mL)	tocopherol (mg/mL)	oxytetracycline (mg/mL)
1	200 LD_{50}	qs	0.25	0.0
2	200 LD_{50}	qs	0.25	8.0
3	200 LD_{50}	qs	0.25	4.0
4	200 LD_{50}	qs	0.25	2.0
5	200 LD_{50}	qs	0.25	1.0
6	200 LD_{50}	qs	0.25	0.5
7	200 LD_{50}	qs	0.25	0.25
8	200 LD_{50}	qs	0.25	0.125
9	200 LD_{50}	qs	(5% $CaCl_2$)	

The number of animals surviving at 0, 18, 25, 42, 48, 72, and 96 hours post administration was counted and recorded. The results demonstrated that a systemically sub-therapeutic amount of oxytetracycline was effective to prevent injection-associated infection by *C. chauveoi*.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

~~WHAT IS CLAIMED:~~

1. A composition suitable for parenteral injection in a bird or mammal, which composition comprises:

an effective amount of a parenterally suitable compound;

a systemically sub-therapeutic amount of an antibiotic; and

a pharmaceutically acceptable carrier.

2. A composition suitable for parenteral injection for inducing estrus in a female mammal, or abortion or parturition in a pregnant mammal, which composition comprises:

an effective amount of a $PGF_2\alpha$ derivative;

a systemically sub-therapeutic amount of an antibiotic; and

a pharmaceutically acceptable carrier.

3. The composition of Claim 2 wherein said $PGF_2\alpha$ derivative is fenprostalene and said antibiotic is oxytetracycline.

4. The composition of Claim 3 wherein said fenprostalene is present in an amount between ~~about~~ 0.25 mg/mL and ~~about~~ 1.0 mg/mL.

5. The composition of Claim 3 wherein said oxytetracycline is present in an amount between ~~about~~ 0.4% and ~~about~~ 1.6%.

6. The composition of Claim 3 which comprises:
0.025% - 0.050% fenprostalene;

0.4% - 1.6% oxytetracycline; and
a pharmaceutically acceptable carrier.

7. The composition of Claim 6 which comprises:
0.025% - 0.050% fenprostalene;
0.025% - 0.050% dl-α-tocopherol;
0.4% - 1.6% oxytetracycline; and
a pharmaceutically acceptable carrier.

8. A method for inducing estrus, abortion, or parturition in a female mammal without initiating infection, which method comprises:
administering a composition containing an effective amount (as herein defined) of a $PGF_2\alpha$ derivative; a systemically sub-therapeutic amount of an antibiotic; and a pharmaceutically acceptable carrier.

9. The method of Claim 8 wherein said $PGF_2\alpha$ derivative is fenprostalene and said antibiotic is oxytetracycline.

10. The composition of Claim 9 wherein said fenprostalene is present in an amount between ~~about~~ 0.25 mg/mL and ~~about~~ 1.0 mg/mL.

11. The composition of Claim 9 wherein said oxytetracycline is present in an amount between ~~about~~ 0.4% and ~~about~~ 1.6%.

12. The method of Claim 9 wherein said composition comprises:
0.025% - 0.050% fenprostalene;
0.4% - 1.6% oxytetracycline; and
a pharmaceutically acceptable carrier.

13. The method of Claim 12 wherein said composition comprises:

0.025% - 0.050% fenprostalene;
0.025% - 0.050% dl-α-tocopherol;
0.4% - 1.6% oxytetracycline; and
a pharmaceutically acceptable carrier.

14. A method for administering a parenterally suitable compound to a bird or mammal without initiating infection, which method comprises:

administering a composition containing an effective amount of a parenterally suitable compound; a systemically sub-therapeutic amount of an antibiotic; and a pharmaceutically acceptable carrier.

15. The method of Claim 14 wherein said parenterally suitable compound is a vaccine, hormone, vitamin, or nutritional supplement.

DATED THIS 16th day of February, 1987.

SYNTEX (U.S.A.) INC.

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