**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobilis Influenza H7N1 emulsion for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose of 0.5ml contains:

**Active substance:**
Inactivated whole avian influenza virus antigen of H7N1 subtype (strain, A/CK/Italy/473/99), inducing an HI titre of $\geq 6.0$ $\log_2$ as tested according to the potency test.

**Adjuvant:**
Liquid light paraffin 234.8 mg/0,5 ml

For a list of excipients see section 6.1

## 3. PHARMACEUTICAL FORM

Emulsion for injection

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Chickens and ducks

### 4.2 Indications for use, specifying the target species

For active immunisation of chickens and ducks against avian influenza type A, subtype H7N1.

Efficacy has been evaluated on the basis of preliminary results in chickens and ringed teals.
-In chickens, reduction of clinical signs, mortality, excretion and transmission of virus after challenge were shown by two weeks after a single dose vaccination.
-In ducks, reduction of excretion and transmission of virus after challenge were shown by two weeks after a single dose vaccination.

Although it has not been investigated with this particular AI vaccine strain, studies performed with other strains show that protective levels of serum antibody titres would be expected to persist in chickens for at least 12 months after administration of two doses of vaccine. The duration of immunity in ducks is unknown.

### 4.3 Contraindications

None.

### 4.4 Special warnings for each target species

This vaccine has been tested for safety in chickens and only supportive data for safety in ducks are available. If used in other avian species that are considered at risk of infection, its use in these species should be undertaken with care and it is advisable to test the vaccine on a small number of birds prior to mass vaccination. The level of efficacy for other species may differ from that observed in chickens. The level of efficacy attained may vary depending on the degree of antigenic homology between the vaccine strain and circulating field strains.

## 4.5 Special precautions for use

Special precautions for use in animals

None

**Special precautions to be taken by the person administering the veterinary medicinal product to animals**

**To the user:**
This product contains mineral oil. Accidental injection/self injection may result in severe pain and swelling, particularly if injected into a joint or finger, and in rare cases could result in the loss of the affected finger if prompt medical attention is not given. If you are accidentally injected with this product, seek prompt medical advice even if only a very small amount is injected and take the package leaflet with you. If pain persists for more than 12 hours after medical examination, seek medical advice again.

**To the physician:**
This product contains mineral oil. Even if small amounts have been injected, accidental injection with this product can cause intense swelling, which may, for example, result in ischaemic necrosis and even the loss of a digit. Expert, PROMPT, surgical attention is required and may necessitate early incision and irrigation of the injected area, especially where there is involvement of finger pulp or tendon.

## 4.6 Adverse Reactions (frequency and seriousness)

Safety has been assessed on the basis of results in chickens. A transient diffuse swelling may occur at the vaccination site in 50% of the animals, which persists for about 14 days.
Supportive data in ducks suggest that minor local swellings may occur at the injection sites but disappear within 3 weeks.

## 4.7 Use during pregnancy, lactation or lay

No information is available on the safety of this vaccine for birds in lay.

## 4.8 Interactions with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

## 4.9 Amounts to be administered and administration route

Allow the vaccine to reach a temperature of 15°C - 25°C and shake well before use.
Use sterile syringes and needles.
It is recommended to use a closed multidose vaccination system.

***Chickens***

From 8 to 14 days old: 0.25 ml subcutaneously

From 14 days to 6 weeks old: 0.25 or 0.5 ml subcutaneously or intramuscularly

6 weeks and older: 0.5 ml subcutaneously or intramuscularly

Future laying hens and breeders should get a second vaccination 4-6 weeks after first vaccination.

No information is available on vaccination in the presence of maternally derived antibodies. Immunisation of progeny from vaccinated birds should therefore be delayed until such antibodies have declined.

***Ducks***

From 2 to 6 weeks: 0.5 ml subcutaneously or intramuscularly.
Laying and breeder stock should get a second vaccination 6-10 weeks after the first vaccination. A dose of 1 ml is advised.

### 4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Following the administration of a double dose no adverse reactions other than those described in section 4.6 have been observed.

### 4.11 Withdrawal period(s)

Zero days.

## 5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: inactivated vaccine, ATC-vet code: QI01AA23

The vaccine stimulates active immunity against Avian Influenza virus type A, subtype H7N1.

If the circulating avian influenza field virus has a different H and/or N component to the H7N1 included in the vaccine, it may be possible to differentiate between vaccinated and infected birds by using a diagnostic test to detect haemagglutinin and/or neuraminidase antibodies.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Liquid light paraffin
Polysorbate 80
Sorbitane mono-oleate
Glycine

### 6.2 Incompatibilities

Do not mix with any other veterinary medicinal product.

### 6.3 Shelf life

PET vials: 2 years
Glass vials: 1 year

After broaching, use within 8 hours, provided the product is not subject to extreme temperatures or contaminated.

### 6.4 Special precautions for storage

Store refrigerated (2°C to 8°C). Do not freeze.

### 6.5 Nature and composition of immediate packaging

250 ml or 500 ml bottles of glass, hydrolytical class type II or of polyethylene terephthalate (PET). The bottles are closed with a nitryl rubber stopper and sealed with a coded aluminium cap.

Not all pack sizes may be marketed.

### 6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products, if appropriate

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

## 8. MARKETING AUTHORISATION NUMBER

EU/2/07/073/001-004

## 9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

14-05-2007

## 10. DATE OF REVISION OF THE TEXT

31.07.2009

## PROHIBITION OF SALE, SUPPLY AND/OR USE

The import, sale, supply and/or use of Nobilis Influenza H7N1 is or may be prohibited in certain Member States on the whole or part of their territory pursuant to national animal health policy. Any person intending to import, sell, supply and/or use Nobilis Influenza H7N1 must consult the relevant Member State's competent authority on the current vaccination policies prior to the import, sale, supply and/or use.

The use of this veterinary medicinal product is only allowed under the particular conditions established by European Community legislation on the control of Avian Influenza.

Detailed information on this product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu

**ANNEX II**

**A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE**

**B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE**

**C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO SAFE AND EFFECTIVE USE**

**D. STATEMENT OF THE MRLs**

**E. SPECIFIC OBLIGATIONS TO BE FULFILLED BY THE MARKETING AUTHORISATION HOLDER**

## A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Intervet International BV
Wim de Korverstraat 35
NL-5831 AN Boxmeer
The Netherlands

Laboratorios Intervet SA
Poligono El Montalvo
Apartado 3006
Salamanca 37080
Spain

Name and address of the manufacturer responsible for batch release

Intervet International BV
Wim de Korverstraat 35
NL-5831 AN Boxmeer
The Netherlands

## B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE

To be supplied only on veterinary prescription.

According to Article 71 of Directive 2001/82/EC of the European Parliament and of the Council as amended, Member States prohibit or may prohibit the import, sale, supply and/or use of the veterinary medicinal product on the whole or part of their territory if it is established that:

a) the administration of the veterinary medicinal product to animals will interfere with the implementation of national programmes for the diagnosis, control and eradication of animal diseases, or will cause difficulties in certifying the absence of contamination in live animals or in foodstuffs or other products obtained from treated animals.

b) the disease to which the veterinary medicinal product is intended to confer immunity is largely absent from the territory.

The use of this veterinary medicinal product is only allowed under the particular conditions established by European Community legislation on the control of Avian Influenza.

The holder of this marketing authorisation must inform the European Commission about the marketing plans for the medicinal product authorised by this decision.

## C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO SAFE AND EFFECTIVE USE

Not applicable.

## D. STATEMENT OF THE MRLs

The following substances contained in the final product are included in Annex II of Council Regulation (EEC) No 2377/90:

| Pharmacologically active substance | Animal Species | Other provisions |
|---|---|---|
| Light liquid paraffin | All food producing species | |
| Polysorbate 80 | All food producing species | |
| Sorbitan mono oleate (E494) | All food producing species | |
| Glycine | All food producing species | |

## E. SPECIFIC OBLIGATIONS TO BE FULFILLED BY THE MARKETING AUTHORISATION HOLDER

The Marketing Authorisation Holder shall complete the following programme of studies within the specified time frame, the results of which shall form the basis of the annual reassessment of the benefit/risk profile.

### II. ANALYTICAL ASPECTS

### II.C. STARTING MATERIALS

### II.C.2 Not listed in a Pharmacopoeia

1. Tryptose: The Applicant should provide a list of any changes to the source countries for the pigs used as a source of the porcine starting material in tryptose.

**Specific Measures concerning the prevention of the transmission of animal spongiform encephalopathies**

2. A revised supporting TSE compliance table should be provided with deletion of the words 'or equivalent' after the source companies for the tryptose and NZ-Amines and 'e.g.' before the corresponding lists of source countries.
3. An up-to-date certificate of suitability should be provided for Rousselot Acid hide gelatin (European origin)

### II.E. CONTROL TESTS ON THE FINISHED PRODUCT

### II.E.2 Identification and assay of active ingredients

4. Batch potency test:

A clear justification should be given in support of the proposed pass level of an HI serum titre of 6.0 $\log_2$.

### II. F. STABILITY

### II.F.1 Stability of the bulk antigen

5. The antigen should be stored for no longer than 12 months at 2-8ºC pending the provision of data supporting a longer period of storage.

### SAFETY ASPECTS

6. The report of the overdose safety studies in ducks with Nobilis Influenza H7N1 administered by both s.c. and i.m. routes should be provided as soon as it is available

**PHARMACOVIGILANCE ASPECTS**

7. The applicant is required to submit 3-montly Periodic Update Safety reports for the first 2 years following the initial use in the field and is additionally required to present a protocol that would ensure adequate recording and reporting of field data in relation to suspected adverse reactions including suspected lack of efficacy.

**EFFICACY ASPECTS**

8. Batch release data for all batches of H7N1 vaccine used in the efficacy trials presented in the dossier and justification for the potency release criteria should be provided. The distinction between what might be protective titres of antibodies and the level of antibodies generated under the conditions of the batch potency test should be taken into account and the minimum potency at the time of batch release should be sufficient to provide the claimed duration of immunity.

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

**A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**CARTON**
**{250ml Bottle / 500ml Bottle}**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobilis Influenza H7N1
Emulsion for injection

## 2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

One dose of 0.5 ml contains:
Inactivated whole avian influenza virus antigen of H7N1 subtype (strain, A/CK/Italy/473/99), inducing an HI titre of $\geq 6.0$ $\log_2$ as tested according to the potency test.

**Adjuvant:**
Liquid light paraffin 234.8 mg/0.5 ml

## 3. PHARMACEUTICAL FORM

Emulsion for injection

## 4. PACKAGE SIZE

250 ml
500 ml

## 5. TARGET SPECIES

Chickens and ducks

## 6. INDICATION(S)

Active immunisation against avian influenza type A, subtype H7N1.

## 7. METHOD AND ROUTE(S) OF ADMINISTRATION

I.M. or S.C. injection of 0.25, 0.5 ml or 1 ml, depending on the age and species.
Read the package leaflet before use.

## 8. WITHDRAWAL PERIOD

Withdrawal period - Zero days

## 9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

## 10. EXPIRY DATE

<EXP {month/year}>
Once broached, use within 8 hours.

## 11. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated (2°C to +8°C). Do not freeze.

## 12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Read the package leaflet before use.

## 13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.

The use of this veterinary medicinal product is only allowed under the particular conditions established by European Community legislation on the control of Avian Influenza.

## 14. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

## 15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

## 16. MARKETING AUTHORISATION NUMBER(S)

EU/2/07/073/001-004

## 17. MANUFACTURER'S BATCH NUMBER

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING**

**BOTTLE LABEL**
**{250ml/500ml}**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobilis Influenza H7N1
Emulsion for injection

## 2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

One dose of 0.5 ml contains:
Inactivated whole avian influenza virus antigen of H7N1 subtype (strain, A/CK/Italy/473/99), inducing an HI titre of $\geq 6.0$ $\log_2$ as tested according to the potency test.

**Adjuvant:**
Liquid light paraffin 234.8 mg/0.5 ml

## 3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

250 ml
500 ml

## 4. ROUTE(S) OF ADMINISTRATION

I.M. or S.C. injection
Read the package leaflet before use.

## 5. WITHDRAWAL PERIOD

Withdrawal period: Zero days

## 6. BATCH NUMBER

<Lot> {number}

## 7. EXPIRY DATE

<EXP {month/year}>
Once broached, use within 8 hours.

## 8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

**B. PACKAGE LEAFLET**

**PACKAGE LEAFLET FOR:**

**Nobilis Influenza H7N1**
**emulsion for injection**

## 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Manufacturer for the batch release:

Intervet International BV
Wim de Körverstraat 35
NL-5831 AN Boxmeer
The Netherlands

## 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobilis Influenza H7N1
Emulsion of injection

## 3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

On dose of 0.5 ml contains:
Inactivated whole avian influenza virus antigen of H7N1 subtype (strain, A/CK/Italy/473/99), inducing an HI titre of $\geq 6.0$ $\log_2$ as tested according to the potency test.

Adjuvant: Liquid paraffin

## 4. INDICATION

For active immunisation of chickens and ducks against avian influenza type A, subtype H7N1.

Efficacy has been evaluated on the basis of preliminary results in chickens and ringed teals.
-In chickens, reduction of clinical signs, mortality, excretion and transmission of virus after challenge were shown by two weeks after a single dose vaccination.
-In ducks, reduction of excretion and transmission of virus after challenge were shown by two weeks after a single dose vaccination.

Although it has not been investigated with this particular AI vaccine strain, studies performed with other strains show that protective levels of serum antibody titres would be expected to persist in chickens for at least 12 months after administration of two doses of vaccine. The duration of immunity in ducks is unknown.

## 5. CONTRAINDICATIONS

None.

## 6. ADVERSE REACTIONS

Safety has been assessed on the basis of results in chickens. A transient diffuse swelling may occur at the vaccination site in 50% of the animals, which persists for about 14 days.
Supportive data in ducks suggest that minor local swellings may occur at the injection sites but disappear within 3 weeks.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

## 7. TARGET SPECIES

Chickens and ducks

## 8. DOSAGE FOR EACH SPECIES, ROUTES AND METHOD OF ADMINISTRATION

*Chickens*
From 8 to 14 days old: 0.25 ml subcutaneously

From 14 days to 6 weeks old: 0.25 or 0.5ml subcutaneously or intramuscularly

6 weeks and older: 0.5ml subcutaneously or intramuscularly

Future laying hens and breeders should get a second vaccination 4-6 weeks after first vaccination

No information is available on vaccination in the presence of maternally derived antibodies. Immunisation of progeny from vaccinated birds should therefore be delayed until such antibodies have declined.

*Ducks*

From 2 to 6 weeks: 0.5 ml subcutaneously or intramuscularly.
Laying and breeder stock should get a second vaccination 6-10 weeks after the first vaccination. A dose of 1 ml is advised.

## 9. ADVICE ON CORRECT ADMINISTRATION

Allow the vaccine to reach a temperature of 15°C-25°C and shake well before use.
Use sterile syringes and needles. It is recommended to use a closed multidose vaccination system.

## 10. WITHDRAWAL PERIOD

Zero days

## 11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
Store and transport at 2°C to 8°C. Do not freeze.
After broaching, use within 8 hours, provided the product is not subject to extreme temperatures or contaminated.
Do not use after the expiry date which is stated on the label.

## 12. SPECIAL WARNINGS

This vaccine has been tested for safety in chickens and only supportive data for safety in ducks are available. If used in other avian species that are considered at risk of infection, its use in these species should be undertaken with care and it is advisable to test the vaccine on a small number of birds prior to mass vaccination. The level of efficacy for other species may differ from that observed in chickens. The level of efficacy attained may vary depending on the degree of antigenic homology between the vaccine strain and circulating field strains.

No information is available on the safety of this vaccine for birds in lay.

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

Do not mix with any other veterinary medicinal product.

Special warning for the user:
This product contains mineral oil. Accidental injection/self injection may result in severe pain and swelling, particularly if injected into a joint or finger, and in rare cases could result in the loss of the affected finger if prompt medical attention is not given. If you are accidentally injected with this product, seek prompt medical advice even if only a very small amount is injected and take the package leaflet with you. If pain persists for more than 12 hours after medical examination, seek medical advice again.

To the physician:
This product contains mineral oil. Even if small amounts have been injected, accidental injection with this product can cause intense swelling, which may, for example, result in ischaemic necrosis and even the loss of a digit. Expert, PROMPT, surgical attention is required and may necessitate early incision and irrigation of the injected area, especially where there is involvement of finger pulp or tendon.

## 13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

31.07.2009

Detailed information on this product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu

## 15. OTHER INFORMATION

If the circulating avian influenza field virus has a different H and/or N component to the H7N1 included in the vaccine, it may be possible to differentiate between vaccinated and infected birds by using a diagnostic test to detect haemagglutinin and/or neuraminidase antibodies.

The use of this veterinary medicinal product is only allowed under the particular conditions established by European Community legislation on the control of Avian Influenza.

Pack sizes:
250 or 500 ml multidose glass bottle
250 or 500 ml multidose PET bottle
The bottles are closed with a rubber stopper and an aluminium cap.

Not all pack sizes may be marketed.