ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Folltropin 700 IU Powder and Solvent for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial of lyophilized product contains:
Active substance:
Follicle Stimulating Hormone (FSH) 700 IU

One vial of solvent contains:
Excipient:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	360 mg

One ml of reconstituted solution contains:
Active substance:
Follicle Stimulating Hormone (FSH) 35 IU

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	18 mg
Water for Injections	
Sodium Chloride	
Sodium hydroxide	
Hydrochloric acid	

Powder: Freeze dried off-white to slightly pink powdered cake
Solvent: Clear, colourless solution
Reconstituted solution: Clear, slightly pink solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (reproductively mature females).

3.2 Indications for use for each target species

To induce superovulation in reproductively mature heifers or cows.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in males and reproductively immature female cattle.
Do not use in pregnant cattle.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

The product should only be used in clinically healthy cows and mature heifers, which are cycling normally. There is a wide range in response to superovulation between animals. There may be a small proportion of non-responders in any group treated.

Collection of embryo is normally started on day 7 following observed oestrus or first breeding. Prior to breeding and the collection of fertilized embryo from these animals, oestrus will have to be induced with prostaglandin F2α or a prostaglandin F2α analogue.

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

Care should be taken when handling the product to avoid self-injection. Accidental self-injection of FSH may cause biological effects in women and to the unborn child. In case of accidental self- injection in women who are pregnant, or whose pregnancy status is unknown, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Target species: cattle (reproductively mature females).

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Ovarian cyst*, lack of heat**

* Following administration for three superovulation cycles, but did not prevent pregnancy.

** Following superovulation a delayed return to heat is possible.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:

Laboratory studies with FSH in rats and rabbits have shown evidence of embryotoxicity/foetotoxicity. The safety of the veterinary medicinal product has not been established during pregnancy. Do not use in pregnant cattle.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

For intramuscular administration only.

Dissolve each vial of freeze-dried product with the enclosed solvent. Reconstitution and subsequent withdrawal of product should be performed using strict aseptic technique.

Regimen:

Start injections on day 8 to 10 following observed or induced oestrus. Administer 2.5 ml (87 .5 I.U.) of the product intramuscularly, twice daily, for 4 days. In conjunction with the 6th dose of the product, administer prostaglandin F2α or a prostaglandin F2α analogue, at their manufacturer's recommended dose, to cause luteolysis.

Inseminate animals at 12 and 24 hours after the onset of oestrus or 60 and 72 hours after prostaglandin treatment. Additional inseminations may be conducted at 12 hour intervals if indicated.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Cows were able to respond to the product consistently throughout a series of 3 treatments. No adverse reactions were detected in treated cows after the injection of 400 mg of the product as a single dose.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Meat and offal: Zero days.
Milk: Zero hours.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:
QG03GA90

4.2 Pharmacodynamics

Follicle Stimulating Hormone from an extract of porcine pituitary glands for use in cattle.

FSH is the initiator of ovarian activity since it directly promotes growth of ovarian follicles. The administration of exogenous FSH to mammals at the time of follicular wave emergence stimulates growth of all follicles over 1.7 mm diameter which would normally be lost to atresia during each oestrus cycle. Multiple growing follicles require FSH stimulation until they are mature enough to respond to LH for the final stages of maturation and ovulation. This usually takes a period of approximately 4 days. In cattle, fertilised ova produced by superovulation with FSH, PMSG and other pharmacological agents containing high concentrations of LH have shown reduced fertilisation. The productcontains porcine pituitary extract with FSH activity and low LH activity.

4.3 Pharmacokinetics

When administered by intramuscular injection, FSH of porcine origin is rapidly absorbed from the site of injection. It has a half-life of 5 hours and FSH cannot be detected in the blood stream 12 hours after injection. FSH is inactivated by the liver and then excreted by the kidneys.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product except the solvent supplied for use with the veterinary medicinal product.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: Freeze-dried powder and solvent vials: 4 years.

Shelf-life after reconstitution according to directions: 4 days.

5.3 Special precautions for storage

Freeze dried powder and solvent vials: Do not store above 25ºC.

Reconstituted solution: Store in a refrigerator (2 - 8ºC).

Keep the vials in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Cardboard box containing one vial of powder and one vial of 20 ml of solvent.

Freeze-dried powder
Clear glass 20 ml vial (Type I), with halobutyl rubber stopper (Type I) and red flip-off cap.

Solvent
Clear glass 20 ml vial (Type I), with halobutyl rubber stopper (Type I) and yellow flip-off cap.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

7. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: To be completed nationally.

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

To be completed nationally.

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Folltropin 700 IU Powder and Solvent for Solution for Injection

2. STATEMENT OF ACTIVE SUBSTANCE

Powder vial: 700 IU FSH

3. PACKAGE SIZE

1 powder vial and 1 solvent vial

4. TARGET SPECIES

Cattle (reproductively mature females).

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

For intramuscular use only.

7. WITHDRAWAL PERIODS

Withdrawal periods:
Meat and offal: Zero days.
Milk: Zero hours.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once reconstituted, use within 4 days.

9. SPECIAL STORAGE PRECAUTIONS

Freeze-dried powder and solvent vials: Do not store above 25€.
Reconstituted solution: store in a refrigerator (2 - 8ºC).
Keep the vials in the outer carton in order to protect from light.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally.

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

CLEAR GLASS 20ML VIAL (FSH)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Folltropin

2. STATEMENT OF ACTIVE SUBSTANCES

Each 20ml vial contains FSH equivalent to 700 IU

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once reconstituted, use within 4 days.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

CLEAR GLASS 20ML VIAL (SOLVENT)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Folltropin solvent for solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

20ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Folltropin 700 IU Powder and Solvent for Solution for Injection.

2. Composition

Powder vial contains:
Active substance
Follicle Stimulating Hormone (FSH) 700 IU

Solvent vial contains:
Excipients
Benzyl alcohol 360 mg

One ml of reconstituted solution contains:
Active substance:
Follicle Stimulating Hormone (FSH) 35 IU
Excipients
Benzyl alcohol 18 mg

Powder: Freeze dried off-white to slightly pink powdered cake
Solvent: Clear, colourless solution
Reconstituted solution: Clear, slightly pink solution.

3. Target species

Cattle (reproductively mature females).

4. Indications for use

To induce superovulation in reproductively mature heifers or cows.

5. Contraindications

Do not use in males, in reproductively immature or pregnant cattle or in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special precautions for safe use in the target species:

The product should only be used in clinically healthy cows and mature heifers, which are cycling normally. There is a wide range in response to superovulation between animals. There may be a small proportion of non-responders in any group treated.

Collection of embryo is normally started on day 7 following observed oestrus or first breeding. Prior to breeding and the collection of fertilized embryo from these animals, oestrus will have to be induced with prostaglandin F2α or a prostaglandin F2α analogue.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Care should be taken when handling the product to avoid self-injection. Accidental self-injection of FSH may cause biological effects in women and to the unborn child. In case of accidental self- injection in women who are pregnant, or whose pregnancy status is unknown, seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy:
Laboratory studies with FSH in rats and rabbits have shown embryotoxicity/foetotoxicity. The safety of the product has not been assessed in pregnant cattle. Do not use in pregnant cattle.

Overdose:
Cows were able to respond to the product consistently throughout a series of 3 treatments. No adverse reactions were detected in treated cows after the injection of 400 mg of the product as a single dose.

Major incompatibilities:
Do not mix with any other veterinary medicinal product except the solvent supplied for use with the veterinary medicinal product.

7. Adverse events

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Ovarian cyst*, lack of heat**

* Following administration for three superovulation cycles, but did not prevent pregnancy

** Following superovulation a delayed return to heat is possible

No adverse reactions were detected in cows after injecting 400 mg as a single dose.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.'

8. Dosage for each species, routes and method of administration

For intramuscular administration only.

Dissolve each vial of freeze-dried product with the enclosed solvent.

Regimen:

Start injections on day 8 to 10 following observed or induced oestrus. Administer 2.5 mL (87.5 I.U.) of the product intramuscularly, twice daily, for 4 days. In conjunction with the 6th dose of the product, administer prostaglandin F2α or a prostaglandin F2α analogue, at their manufacturer's recommended dose, to cause luteolyesis.

Breed animals at 12 and 24 hours after the onset of oestrus or 60 and 72 hours after prostaglandin treatment. Additional inseminations may be conducted at 12 hours intervals.

9. Advice on correct administration

Dissolve the product only with the solvent provided. Use strict aseptic technique when preparing and withdrawing the product.

10. Withdrawal periods

Meat and offal: Zero days.
Milk: Zero hours.

11. Special storage precautions

Keep out of the sight and reach of children.

Freeze-dried powder and solvent vials: Do not store above 25 €.
Reconstituted solution: store in a refrigerator (2 - 8€)
Keep the vials in the outer carton in order to protect from light.
Shelf life following reconstitution according to directions: 4 days.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.
When the product is reconstituted, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.
Do not freeze after mixing. Discard any unused portion of the reconstituted solution.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

To be completed nationally.
Pack Sizes: Cardboard box containing one vial of powder and one vial of 20 ml of solvent.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

To be completed nationally.
Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder:

To be completed nationally.

Manufacturer responsible for batch release:

Vetoquinol S.A.
Magny-Vernois
70200 Lure
France

Local representatives and contact details to report suspected adverse reactions:
To be completed nationally.

17. Other Information

To be completed nationally.

Day 55 CMS Comments:

NATIONAL ISSUES.

SPC

QUESTION No. 1.	**UK(NI)**

6. NAME OF THE MARKETING AUTHORISATION HOLDER
The name of the Marketing Authorisation Holder in the UK (NI) is Vetoquinol UK Ltd not Vetoquinol Ireland Limited. This change should also be made in the product literature.

APPLICANT'S RESPONSE
The applicant agrees. This paragraph is to be completed nationally.

RMS COMMENTS
National issue.

QUESTION No. 2.	**UK(NI)**

7. MARKETING AUTHORISATION NUMBER(S)
It should be noted that the NI product will be allocated new MA number as a result of this variation. The SPC should be updated with the new UK (NI) MA numbers: 08007/3004.
This change should also be made in the product literature.'

APPLICANT'S RESPONSE
Point well noted.

RMS COMMENTS
National issue.

QUESTION No. 3.	**UK(NI)**

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS
For UK(NI) only: Find more product information by searching for the 'Product Information Database' or 'PID' on www.gov.uk.

APPLICANT'S RESPONSE
Point well noted.

RMS COMMENTS
National issue.

Labelling

QUESTION No. 4.	**UK(NI)**

The applicant is reminded that satisfactory colour mock-ups or artwork of these items will be required before final issue of the Marketing Authorisation in the UK.

APPLICANT'S RESPONSE
Point well noted.

RMS COMMENTS
National issue.

Package leaflet

QUESTION No. 5.	**UK(NI)**

12. Special precautions for disposal
National issue. The disposal wording described in the EU SPC/QRD template (V.9) is not entirely accurate for UK(NI) since advice not to dispose of veterinary medicines via household waste is not appropriate for UK(NI). Therefore, the wording 'or household waste' should not be included on the mock-ups during the national phase for UK(NI). This particular sentence should instead read:

'Medicines should not be disposed of via wastewater.'

APPLICANT'S RESPONSE
Point well noted.

RMS COMMENTS
National issue.

QUESTION No. 6.	**UK(NI)**

15. Date on which the package leaflet was last revised
For UK(NI) only: Find more product information by searching for the 'Product Information Database' or 'PID' on www.gov.uk.

APPLICANT'S RESPONSE
Point well noted.

RMS COMMENTS
National issue.

QUESTION No. 7.	**UK(NI)**

16. Contact details
For UK(NI) only: The registered place of business of the MAH are as follows:
Vetoquinol UK Limited
Steadings Barn
Pury Hill Business Park
Nr Alderton
Towcester
Northants
NN12 7LS

APPLICANT'S RESPONSE
The applicant agrees.

RMS COMMENTS
National issue.

QUESTION No. 8.	**UK(NI)**

The applicant should state UK(NI) local representative and contact details to report suspected Adverse reactions in this section.

APPLICANT'S RESPONSE
The applicant agrees.

RMS COMMENTS
National issue.

QUESTION No. 9.	**PL**

SPC - Sections 6, 7, 8 and 9
The applicant is asked to leave these sections blank, as the information will be different in CMS Poland. The same request is applicable to the corresponding sections of the labelling and package leaflet.

APPLICANT'S RESPONSE
The applicant agrees.

RMS COMMENTS
Noted.

QUESTION No. 10.	**PL**

PACKAGE LEAFLET

16. Contact details

Please note that in CMS Poland the MAH's and local representative's details, if applicable, will be different than stated in this section. The content of this section should take into consideration national differences and to leave room to be completed nationally.

APPLICANT'S RESPONSE
The applicant agrees.

RMS COMMENTS
National issue.

QUESTION No. 11.	**PL**

17. Other Information

Please note that in CMS Poland this section will be left blank.

APPLICANT'S RESPONSE
The applicant agrees.

RMS COMMENTS
National issue.

QUESTION No. 12.	**MAH**

Additional question:

LABEL:
The application would like to propose to keep «i.m.» and «20ml» when the remaining space is available as it is useful information for the end user.

RMS COMMENTS
Please refer to RMS comments above where outstanding issues have been identified.

QUESTION No. 13.	**MAH**

Additional question:

LABEL:

The application would like to propose to delete “once reconstituted, use within 4 days” on the solvent vial label as the reconstitution will be done in the FSH vial.

RMS COMMENTS

Issue resolved.