ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

MULTIMIN Solution for Injection for Cattle
MULTIMIN Vet (FI & SE)
MULTIMIN, Solution for Injection for Cattle (EE, LV, IT & HR)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains

Active substances:
Zinc: 60 mg,
(equivalent to zinc oxide: 74.68 mg)
Manganese: 10 mg,
(equivalent to manganese carbonate: 20.92 mg)
Copper: 15 mg,
(equivalent to copper carbonate: 26.09 mg)
Selenium: 5 mg,
(equivalent to sodium selenite: 10.95 mg)

Excipients:
Benzyl alcohol (E1519) 10.4mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Clear blue solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle.

4.2 Indications for use, specifying the target species

Supply of trace minerals to correct concurrent clinical or subclinical deficiencies of selenium, copper, manganese and zinc which can arise during critical phases of the production or breeding life cycle.

4.3 Contraindications

Do not administer intramuscularly.

Do not use in cases of known hypersensitivity to the active substances or to any of the excipients.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Additional copper, zinc, manganese or selenium should not be administered at the same time.

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

- This product is HIGHLY concentrated in Selenium.
- Due to a potential risk of Selenium toxicity, care should be taken when handling the product to avoid accidental self-injection.
- The most common manifestations of accidental exposure to selenium in humans are gastrointestinal and neurological symptoms, such as nausea, vomiting, tenderness, fatigue and irritability.
- When treating a large number of animals, a safe injection system should be used.
- Do not work alone when using the product.
- Ensure that animals are properly restrained, including those in the vicinity.
- In case of accidental self-injection, SEEK MEDICAL ADVICE IMMEDIATELY and show the package leaflet or the label to the physician
- Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Mild pain is commonly observed during injection and can persist for up to eight hours after injection. Local reactions at the injection site are very common and consist of transient moderate to severe swelling that can persist for approximately 7 days and evolves into induration estimated at less than 5 cm at palpation after 14 days.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports

4.7 Use during pregnancy, lactation or lay

Pregnancy and Lactation:

Can be used during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Strictly for subcutaneous administration only.
Use standard aseptic procedures during administration of injections.
Strict adherence to correct subcutaneous injection technique should be employed.

Dose:

- Cattle - Up to 1 year: 1ml per 50kg
- Cattle - From 1-2 years: 1ml per 75kg
- Cattle - Over 2 years: 1ml per 100kg

Schedule of administration:

To be administered as a single administration during, or in advance of, periods of stress in the production and breeding life cycle likely to result in concurrent clinical or subclinical deficiencies of the four trace minerals (for example, transport/shipping, calving, breeding).

Maximal volume per injection site: 7ml

The 500ml vial can be broached a maximum of 90 times.

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

No systemic adverse reactions were observed after repeated overdosing (3 consecutive daily administrations) at one to three times the recommended dose (i.e. 3x – 9x recommended dose).

In one study, repeated overdosing (3 consecutive daily administrations) at 5.6xthe recommended dose (i.e., 16.7x recommended dose) is associated with elevation of liver enzymes and hepatic centrilobular necrosis in six animals out of eight, with mortality in one animal.

4.11 Withdrawal period(s)

Meat and offal: 28 days.
Milk: zero hours.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: mineral supplements.
ATCvet code: QA12CX99.

5.1 Pharmacodynamic properties

Manganese is indispensable for the action of glycotransferase. This enzyme plays a role in the formation of the mucopolysaccharide chondroitin sulphate, which is a component of cartilage and due to its action on the formation of cartilage, it is also important for bone formation. Mn is an important component of Mn superoxide dismutase enzyme used in the enzymatic antioxidant system. Although manganese is also part of pyruvic carboxylase and several other enzymes, other divalent cations may serve as alternatives for its role in the activity of these enzymes.

Copper forms an integral part of a number of metalloproteins notably caeruloplasmin, monoamine oxidase, lysyl oxidase, cytochrome C and superoxide dismutase enzymes.

Zinc acts as a cofactor of numerous enzymes, e.g. alcohol dehydrogenase, carbonic anhydrase and carboxypeptidase. Zn is an important component of Zn superoxide dismutase enzyme used in the enzymatic antioxidant system. Zinc plays a role in protein synthesis and cell division. It also exerts crucial influence on the maintenance of cell membrane stability and in the function of the immune system. The connection between the known physiological functions of zinc and the various manifestations of zinc deficiency remain largely unexplained. Zinc interacts with several metabolic ions. Copper, calcium and phytate (a constituent of cereals) reduce zinc absorption; cadmium and zinc compete with each other.

Selenium exerts an antioxidative effect at the cell membrane against hydrogen peroxide and lipoperoxides. The effects are related to enzymatic activity of glutathione peroxidase (GSHPx) which contains selenocysteine. Selenium's protective antioxidative action is partially linked to that of vitamin E. Selenocysteine is also an integral component of other functional proteins e.g. tetra-idothyronine-5-I-deiodinase (involved in metabolism of thyroid hormones) but the full extent of the biochemical mode of action of selenium in the body still remains to be elucidated.

5.2 Pharmacokinetic particulars

Absorption:

- Following subcutaneous administration, the trace minerals are rapidly absorbed from the injection site.

Distribution:

- Once absorbed, manganese is transported to organs rich in mitochondria (in particular the liver, pancreas, and pituitary) where it is rapidly concentrated. The main organ involved in manganese accumulation is the liver which accumulates significantly higher levels of manganese statistically than the kidney. The turnover of manganese in mammalian tissues is rapid.
- Absorbed copper binds to plasma albumin and amino acids in the portal blood and is transported to the liver where it is incorporated into caeruloplasmin and later released into the plasma. Hepatic copper is distributed in several subcellular fractions associated with copper-dependent enzymes and copper-dependent proteins. Copper is also found in erythrocytes in the form of erythrocuprein and other proteins and in bone marrow bound to metallothionein.
- Zinc accumulation is most striking in muscle, followed by the liver, kidney and blood. Zinc values in muscle, liver and kidneys are similar.
- Parenteral selenium is initially transported by serum albumin, after absorption, and later by alpha-2 and beta-1globulin fractions. Selenium is distributed throughout the body, but the highest amounts are present in the liver, kidneys, and muscle.

Metabolism:

- Manganese does not metabolize; it is absorbed and excreted unchanged.
- Copper is available for metabolism by the liver when present as the form bound to albumin. The liver is the major storage organ for copper where it is protein bound, followed by the kidney, muscle and blood.
- After absorption into the body, zinc becomes bound to protein complexes, the most important of which is metallothionein, which acts as a carrier and transport mechanism. As an element zinc is not metabolized per se. Zinc does not accumulate in the body following continued [excessive] exposure.
- The metabolic process involving selenium is dependent on the chemical form and dose as well as on nutritional status. Major metabolites are methylated selenites. Two major metabolic products of selenite have been identified: dimethyl selenide and a trimethylselenonium ion.

Excretion:

- The liver, pancreas, adrenals and intestine play a role in the predominantly faecal excretion of manganese. Small amounts may be excreted in urine. For calves, 21% of an injected dose of manganese is excreted in bile.

- Excess copper is excreted mainly via bile and faeces, though urinary losses account for 0.5% to 3% of the daily intake.
- Excretion of absorbed zinc takes place mainly via bile (80%) and less so via urine and sweat.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Edetic acid
Sodium hydroxide
Water for injections

6.2 Major Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 30 months
Shelf life after first opening the immediate packaging: 28 days

6.4. Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

Primary packaging: Clear Polyethylene Terephthalate (PET) bottle closed with grey bromobutyl rubber stopper sealed with aluminium cap.
Package sizes:

Cardboard box containing one vial of 100 ml

Cardboard box containing one vial of 500 ml

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

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

Warburton Technology Limited,
36 Fitzwilliam Square,
Dublin 2,
IRELAND

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON <THE OUTER PACKAGE> <AND> <THE IMMEDIATE PACKAGE>
Bottle of 100ml and 500ml, Box containing a bottle of 100ml or 500ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

MULTIMIN Solution for Injection for Cattle.

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains
Zinc: 60 mg, (equivalent to zinc oxide: 74.68 mg)
Manganese: 10 mg, (equivalent to manganese carbonate: 20.92 mg)
Copper: 15 mg, (equivalent to copper carbonate: 26.09 mg)
Selenium: 5 mg, (equivalent to sodium selenite: 10.95 mg)

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

Bottle of 100ml
Bottle of 500ml

5. TARGET SPECIES

Cattle

6. INDICATION(S)

Indications for use

Supply of trace minerals to correct concurrent clinical or sub-clinical deficiencies of selenium, copper, manganese and zinc which can arise during critical phases of the production or breeding life cycle.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Strictly for subcutaneous administration only. Do not administer intramuscularly.

Dosage:

- Cattle - Up to 1 year: 1ml per 50kg
- Cattle - From 1-2 years: 1ml per 75kg
- Cattle - Over 2 years: 1ml per 100kg

Schedule of administration

To be administered as a single administration during, or in advance of, periods of stress in the production and breeding life cycle likely to result in concurrent clinical or sub clinical deficiencies of the four trace minerals (for example, transport/shipping, calving, breeding).

Maximal volume per injection site: 7ml

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal Period

Meat and offal: 28 days
Milk: zero hours

9. SPECIAL WARNING(S), IF NECESSARY

Special warnings

Additional copper, zinc, manganese or selenium should not be administered at the same time.
This product is HIGHLY concentrated in Selenium.
Due to a potential risk of Selenium toxicity, care should be taken when handling the product to avoid accidental self – injection.
In case of accidental self – injection, SEEK MEDICAL ADVICE IMMEDIATELY and show the package leaflet or the label to the physician**.**

Read the package leaflet before use.

10. EXPIRY DATE

EXP: {month/year}
Shelf-life after first opening the immediate packaging: 28 days
Once broached, use by……...

11. SPECIAL STORAGE CONDITIONS

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

Dispose of waste material in accordance with local requirements.
This section will be printed on the outer package (carton) only as it is not required on immediate package.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only.

To be supplied only on veterinary prescription

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

Keep out of the sight and reach of children.
This section will be printed on the outer package (carton) only as it is not required on immediate package.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Warburton Technology Limited,
36 Fitzwilliam Square,
Dublin 2,
IRELAND

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch: {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET
MULTIMIN Solution for Injection for Cattle
MULTIMIN Vet (FI & SE)
MULTIMIN, Solution for Injection for Cattle (EE, LV, IT & HR)

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

Marketing authorisation holder:

Warburton Technology Limited
36 Fitzwilliam Square
Dublin 2
IRELAND

Manufacturer responsible for batch release:

LABORATOIRES BIOVE
Rue de Lorraine
B.P. 45
62510 ARQUES
FRANCE

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

MULTIMIN Solution for Injection for Cattle
MULTIMIN Vet (FI & SE)
MULTIMIN, Solution for Injection for Cattle (EE, LV, IT & HR)

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

Each ml contains:

Active substances

Zinc:	60 mg (equivalent to zinc oxide 74.68 mg)
Manganese:	10 mg (equivalent to manganese carbonate 20.92 mg)
Copper:	15 mg (equivalent to copper carbonate 26.09 mg)
Selenium:	5 mg (equivalent to sodium selenite 10.95 mg)

Excipients
Benzyl alcohol (E1519) 10.4 mg

The product is a clear blue solution for injection

4. INDICATION(S)

Supply of trace minerals to correct concurrent clinical or subclinical deficiencies of selenium, copper, manganese and zinc which can arise during critical phases of the production or breeding life cycle.

5. CONTRAINDICATIONS

Do not administer intramuscularly.

Do not use in cases of known hypersensitivity to the active substances or to any of the excipients.

6. ADVERSE REACTIONS

Mild pain is commonly observed during injection and can persist for up to eight hours after injection. Local reactions at the injection site are very common and consist of transient moderate to severe swelling that can persist for approximately 7 days and evolves into induration estimated at less than 5 cm at palpation after 14 days.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s)).
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports

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 inform your veterinary surgeon.
Alternatively, you can report via your national reporting system.

7. TARGET SPECIES

Cattle

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Strictly for subcutaneous administration only.

Doses:

- Cattle - Up to 1 year: 1ml per 50kg
- Cattle - From 1-2 years: 1ml per 75kg
- Cattle - Over 2 years: 1ml per 100kg

Schedule of administration
To be administered as a single administration during, or in advance of, periods of stress in the production and breeding life cycle likely to result in concurrent clinical or subclinical deficiencies of the four trace minerals (for example, transport/shipping, calving, breeding).

Maximal volume per injection site: 7ml

9. ADVICE ON CORRECT ADMINISTRATION

Use standard aseptic procedures during administration of injections.
Strict adherence to correct subcutaneous injection technique should be employed.

The 500ml vial can be broached a maximum of 90 times.

10. WITHDRAWAL PERIOD

Meat and offal: 28 days
Milk: zero hours.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage precautions.

Do not use this veterinary medicinal product after the expiry date which is stated on the bottle and the carton after EXP. The expiry date refers to the last day of that month.

When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the carton should be discarded should be worked out. This discard date should be written in the space provided.

Shelf life after first opening the container: 28 days

12. SPECIAL WARNING(S)

Special precautions for use in animals
Additional copper, zinc, manganese or selenium should not be administered at the same time.

Pregnancy and lactation
Can be used during pregnancy and lactation.

User Warnings
This product is HIGHLY concentrated in Selenium.
Due to a potential risk of Selenium toxicity, care should be taken when handling the product to avoid accidental self – injection.
The most common manifestations of accidental exposure to selenium in humans are gastrointestinal and neurological symptoms, such as nausea, vomiting, tenderness, fatigue and irritability.
When treating a large number of animals, a safe injection system should be used
Do not work alone when using the product.Ensure that animals are properly restrained, including those in the vicinity.
In case of accidental self –injection SEEK MEDICAL ADVICE IMMEDIATELY and show the package leaflet or the label to the physician..
Wash hands after use.

Incompatibilities
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products

Overdose (symptoms, emergency procedures, antidotes):

No systemic adverse reactions were observed after repeated overdosing (3 consecutive daily administrations) at one to three times the recommended dose (i.e. 3x – 9x recommended dose).

In one study, repeated overdosing (3 consecutive daily administrations) at 5.6xthe recommended dose (i.e., 16.7x recommended dose) is associated with elevation of liver enzymes and hepatic centrilobular necrosis in six animals out of eight, with mortality in one animal.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.
Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Primary packaging: Clear polyethylene terephthalate (PET) bottle closed with grey bromobutyl rubber stopper sealed with aluminium cap
Package sizes:

Cardboard box containing one vial of 100 ml

Cardboard box containing one vial of 500 ml

Not all pack sizes may be marketed.

For any information about this veterinary medicinal product, please contact the marketing authorisation holder