ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Frontline Tri-Act 405.6 mg / 3 028.8 mg spot-on solution for dogs 40-60 kg [AT, BG, HR, CY, CZ, EE, FR, DE, EL, HU, IT, LT, LV, MT, NL, PL, PT, RO, ES, SI, SK]
Frontect 405.6 mg / 3 028.8 mg spot-on solution for dogs 40-60 kg [BE, LU]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 6 ml pipette contains:

Active substances:
Fipronil .....405.6 mg
Permethrin .....3 028.8 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Butylhydroxytoluene (E321)	6.750 mg
N-methylpyrrolidone	2 362.2 mg
Medium-chain triglycerides	

Clear colourless to yellow-brown spot-on solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For the treatment and prevention of flea and/or tick infestations where repellent (anti-feeding) activity is necessary against sandflies, biting flies and/or mosquitoes.

- Fleas

Treatment and prevention of *Ctenocephalides felis* flea infestations and prevention of *Ctenocephalides canis* flea infestations. One treatment prevents new flea infestations for 4 weeks.
The veterinary medicinal product can be used as part of a treatment strategy for flea allergy dermatitis where this has been previously diagnosed by a veterinarian.

- Ticks

Treatment and prevention of tick infestations (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus*). One treatment kills (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus*) and repels (*Ixodes ricinus, Rhipicephalus sanguineus)* ticks for 4 weeks after treatment, and repels *Dermacentor reticulatus* from 7 days up to 4 weeks after treatment.

- Mosquitoes and sandflies

Repels (anti-feeding activity) sandflies (*Phlebotomus perniciosus*) for 3 weeks and mosquitoes *(Culex pipiens, Aedes albopictus*) for 4 weeks.
Kills sandflies (*Phlebotomus perniciosus)* and mosquitoes *(Aedes albopictus)* for 3 weeks.
Reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*) for up to 4 weeks. The effect is indirect due to product's activity against the vector.

- Stable flies

Repels (anti-feeding activity) and kills stable flies (*Stomoxys calcitrans*) for 5 weeks.

3.3 Contraindications

Do not use on sick or convalescent animals.
This veterinary medicinal product is for use on dogs only. Do not use in cats and rabbits, as adverse reactions and even death could occur (see section 3.5).
Do not use in cases of hypersensitivity to the active substances or to any of the excipients (see also section 3.5).

3.4 Special warnings

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal.

There may be an attachment of single ticks or bites by single mosquitoes or sandflies. For this reason, transmission of pathogens by these arthropods cannot be completely excluded if conditions are unfavorable. Single ticks may attach and detach within the first 24 hours after infestation and if ticks are present when the veterinary medicinal product is applied not all ticks may be killed within 48 hours after treatment. Immediate protection against sandflies bites is not documented. For the reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*), treated dogs should be kept into a protected environment during the first 24 hours after the initial treatment application.
The veterinary medicinal product remains effective against fleas when treated animals are immersed in water occasionally (*e.g.*, swimming, bathing). However, dogs should not be allowed to swim or be shampooed within 48 hours after treatment. Avoid frequent swimming or shampooing of treated dogs as this may adversely affect maintenance of product effectiveness.
The possibility that other animals in the same household can be a source of re-infestation with fleas and/or ticks should be considered, and these should be treated as necessary with an appropriate product. To aid further in reducing environmental challenge, the additional use of a suitable environmental treatment against adult fleas and their developmental stages could be recommended.

3.5 Special precautions for use

Special precautions for safe use in the target species:
In the absence of specific studies, the use of the veterinary medicinal product is not recommended in dogs younger than 8 weeks of age, or in dogs weighing less than 2 kg.
Care should be taken to avoid contact of the veterinary medicinal product with the dog's eyes.
It is important to make sure that the veterinary medicinal product is applied to an area where the animal cannot lick it off and to make sure that other animals do not lick the treatment sites following application.

Due to the unique physiology of cats which prevents them from metabolizing certain compounds, including permethrin, the veterinary medicinal product can induce potentially fatal convulsions in this species. In case of accidental dermal exposure, wash the cat with shampoo or soap, and seek veterinary advice rapidly. To prevent cats from being accidentally exposed to the veterinary medicinal

product, keep treated dogs away from cats until the application site is dry. It is important to ensure that cats do not groom the site of application on a dog which has been treated with this product. In case of exposure of this type seek veterinary advice immediately.
Do not use in cats and rabbits.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product can cause skin and eye irritation, therefore, avoid contact of the veterinary medicinal product with skin and eyes. Do not open the pipette near or towards the face. In case of ocular exposure or if eyes become irritated during administration, immediately flush the eyes with plenty of water. If ocular irritation persists, seek medical attention. In case of dermal exposure or if skin becomes irritated during administration, immediately wash the skin with plenty of soap and water. If skin irritation persists or recurs, seek medical attention.
People with known hypersensitivity to fipronil and/or permethrin should avoid contact with the veterinary medicinal product.
The veterinary medicinal product is harmful if swallowed. Avoid hand-to-mouth contact. Do not smoke, drink or eat during application. Wash hands after use. If swallowed rinse mouth and seek medical attention if you feel unwell.
Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects. The veterinary medicinal product should not be administered by pregnant women and women suspected of being pregnant. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product by women of childbearing age.
Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.
Keep the stored pipettes in the original blister and once used, the empty pipette should immediately be disposed of appropriately, preventing further access.

Special precautions for the protection of the environment:
The veterinary medicinal product may adversely affect aquatic organisms. Treated dogs should not be allowed to enter surface water for 2 days after treatment.

3.6 Adverse events

Dogs:

Very rare (<1 animal / 10 000 animals treated, including isolated reports):	Application site reactions[1] (skin discolouration, hair loss, itching, reddening). Generalised itching, general hair loss, erythema. Hyperaesthesia[2], muscle tremor[2], ataxia[2], other neurological signs[2]. Hyperactivity[2]. Depression[2], anorexia. Vomiting, hypersalivation.

[1] Transient.
[2] Reversible.

If licking of the application site occurs, transient hypersalivation and emesis may be observed.

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

Fertility, pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in dogs during pregnancy and lactation or in animals intended for breeding.
Use only according to the benefit/risk assessment by the responsible veterinarian.
Laboratory studies using fipronil or permethrin have not produced any evidence of teratogenic or embryotoxic effects.
Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic effects.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

Spot-on use.

Dosage:
The minimum dose is 6.76 mg/kg bw of fipronil, and 50.48 mg/kg bw of permethrin corresponding to one pipette of 6 ml per dog (weighing over 40 and up to 60 kg).
Underdosing could result in ineffective use and may favour resistance development.

Treatment schedule:
The use of the veterinary medicinal product should be based on a confirmed infestation or risk of infestation with fleas and/or ticks when repellent (anti-feeding) activity is also necessary against sandflies and/or mosquitoes and/or biting flies. Depending on the ectoparasite challenge repetition of the treatment might be indicated. In such instances, the interval between two treatments should be at least 4 weeks. For infestations with fleas and/or ticks, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

Method of administration:
To ensure a correct dosage, body weight should be determined as accurately as possible.
Select the appropriate pipette size for the weight of the dog. For dogs over 60 kg, use the appropriate combination of two pipette sizes that most closely matches the bodyweight.

The veterinary medicinal product should be applied in two out-of-reach spots so that the dog cannot lick the application site. These sites are at the base of the neck in front of the shoulder blades and the middle of the neck between the base of the skull and the shoulder blades.

Remove the blister card from the package and separate one blister. Remove the pipette by cutting along the dotted line with a pair of scissors or tearing open after folding the marked corner. Holding the pipette upright away from face and body, cut the pipette tip with scissors to open. Part the coat on the back of the dog until the skin is visible. Place the tip of the pipette on the skin. Squeeze the pipette, applying about half of the content halfway down the neck between the base of the skull and the shoulder blades. Repeat the application at the base of the neck in front of the shoulder blades to empty the pipette. For best results, ensure that the veterinary medicinal product is applied directly to the skin rather than on the hair.

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

Safety has been assessed with up to 5 times the maximum dose in healthy adult dogs (treated up to 3 times at monthly intervals) and in puppies (aged 8 weeks treated once). Known side-effects may consist of mild neurological signs, emesis and diarrhea. These are transitory and generally resolve without treatment within 1-2 days.

The risk of experiencing adverse events (see section 3.6) may increase with overdosing, so animals should always be treated with the correct pipette size according to bodyweight.

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

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP53AX65

4.2 Pharmacodynamics

Fipronil is an insecticide and acaricide belonging to the phenylpyrazole family. Fipronil and its metabolite fipronil sulfone act at ligand-gated chloride channels, in particular those gated by the neurotransmitter gamma-aminobutyric acid (GABA) as well as desensitising (D) and non-desensitising (N) channels gated by glutamate (Glu, unique invertebrate ligand-gated chloride channels), thereby blocking pre- and post-synaptic transfer of chloride ions across cell membranes. This results in uncontrolled activity of the central nervous system and death of arthropods.

Permethrin belongs to the Type I class of pyrethroids, which are acaricides and insecticides with repellent activity. Pyrethroids affect the voltage-gated sodium channels in vertebrates and non-vertebrates. Pyrethroids are so-called "open channel blockers" affecting the sodium channel by slowing both the activation and the inactivation properties, thus leading to hyper-excitability and death of the parasite. Permethrin in the product provides repellent activity (anti-feeding activity) against sandflies (*Phlebotomus perniciosus*, > 90% for 3 weeks and > 80% for an additional week), mosquitoes (*Culex pipiens, Aedes albopictus*) and ticks (*Ixodes ricinus*, *Dermacentor reticulatus*, *Rhipicephalus sanguineus*).
In one experimental study, the product had a faster onset on flea adulticidal activity than fipronil alone at 7 and 14 days after treatment administration.

Speed of kill:
The product kills new infesting fleas (*C. canis, C. felis*) within 6 hours from 2 days after treatment and for a full month. The product kills fleas before they can lay eggs, preventing dog's environment contamination. In case of pre-existing infestation (*C. felis*), the product will take 24 hours to effectively start to disrupt the flea life cycle.. *C. felis* fleas already present on dogs when the treatment is applied are killed in 24 hours. Speed of kill against pre-existing *C. canis* has not been evaluated.
The product kills new infesting ticks (*R. sanguineus* and *I. ricinus*) within 6 hours from 2 days after treatment and for a full month. Ticks (*R. sanguineus, I. ricinus, D. reticulatus*) already present on dogs when the treatment is applied are killed in 48 hours.

In one experimental study, the product was shown to indirectly reduce the risk of transmission of *Babesia canis* from infected *Dermacentor reticulatus* ticks from 7 days after application up to 4 weeks, thereby reducing the risk of canine babesiosis in treated dogs in this study.

In one experimental study, the product was shown to indirectly reduce the risk of transmission of *Ehrlichia canis* from infected *Rhipicephalus sanguineus* ticks, from 7 days after application up to 4 weeks, thereby reducing the risk of ehrlichiosis in treated dogs in this study.
However, the effectiveness of the product at reducing the transmission of these infectious agents following natural exposure under field conditions has not been investigated.
In one preliminary and one pivotal clinical field studies in an endemic area, the product applied every 4 weeks was shown to indirectly reduce the risk of transmission of *Leishmania infantum* from infected sandflies (*Phlebotomus perniciosus*), thereby reducing the risk of canine leishmaniosis in treated dogs in these studies.

4.3 Pharmacokinetics

The pharmacokinetic profiles of fipronil and permethrin in combination were studied after topical application in dogs by measuring plasma and hair concentrations for 58 days following treatment.
Both permethrin and fipronil, together with its major metabolite, fipronil sulfone, are well-distributed on the haircoat of a dog during the first day after application. The concentrations of fipronil, fipronil sulfone and permethrin in the hair coat decrease with time and are detectable for at least 58 days after dosing.
Fipronil and permethrin act topically upon contact with external parasites and the low systemic absorption of fipronil and permethrin is not relevant for the clinical efficacy.
The spot-on application resulted in negligible systemic absorption of permethrin with sporadic measurable concentrations of cis-permethrin between 11.4 ng/ml and 33.9 ng/ml observed 5 to 48 hours following treatment.
Mean maximum plasma concentrations (Cmax) of 30.1 ± 10.3 ng/ml fipronil and 58.5 ± 20.7 ng/ml of fipronil sulfone were observed between Day 2 and 5 (Tmax) following application. Fipronil plasma concentrations then decline with a mean terminal half-life of 4.8 ± 1.4 days.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

5.3 Special precautions for storage

Store in the original blister.
Do not store above 25°C.

5.4 Nature and composition of immediate packaging

The primary packaging is a heat-formed film of polyethylene-ethylvinyl alcohol-polyethylene/polypropylene.
The secondary packaging consists of a plastic/aluminium blister with a plastic/aluminium backing.

Plastic card of 1 pipette containing 6 ml.
Carton box of 3 or 6 pipettes containing 6 ml each.
One size only per box.
Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.
The veterinary medicinal product should not enter water courses as fipronil/permethrin may be dangerous for fish and other aquatic organisms.

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

To be completed nationally.

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

{DD/MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product not subject to prescription: AT, BG, DE, ES, HR, HU, CZ, EE, FR, IT, LV, LT, MT, NL, PL, PT, RO, SK, SL.
Veterinary medicinal product subject to prescription: BE, LU, EL, CY.

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 box of 3 pipettes
Carton box of 6 pipettes
Plastic card of 1 pipette

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Frontline Tri-Act spot-on solution [AT, BG, HR, CY, CZ, EE, FR, DE, EL, HU, IT, LT, LV, MT, NL, PL, PT, RO, ES, SI, SK]
Frontect spot-on solution [BE, LU]

2. STATEMENT OF ACTIVE SUBSTANCES

Each 6 ml pipette contains:
Fipronil 405.6 mg, Permethrin 3 028.8 mg

3. PACKAGE SIZE

1 x 6 ml
3 x 6 ml
6 x 6 ml

4. TARGET SPECIES

Dogs 40-60 kg

Do not use in cats and rabbits.

5. INDICATIONS

For non-prescription status only:
For the treatment and prevention of flea and/or tick infestations where repellent (anti-feeding) activity is necessary against sandflies, biting flies and/or mosquitoes. Reduction of the risk of infection with *Leishmania infantum*.

Fleas & Ticks + Biting flies, Sandflies & mosquitoes

6. ROUTES OF ADMINISTRATION

Spot-on use.
Cut the pipette tip with scissors to open.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Store in the original blister.
Do not store above 25°C.

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

Blister foil
All presentations

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Frontline Tri-Act [AT, BG, HR, CY, CZ, EE, FR, DE, EL, HU, IT, LT, LV, MT, NL, PL, PT, RO, ES, SI, SK]
Frontect [BE, LU]

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

fipronil
permethrin
40-60 kg

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pipette foil

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Frontline Tri-Act [AT, BG, HR, CY, CZ, EE, FR, DE, EL, HU, IT, LT, LV, MT, NL, PL, PT, RO, ES, SI, SK]
Frontect [BE, LU]

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

6 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET
(Carton box of 3 or 6 pipettes)

1. Name of the veterinary medicinal product

[AT, BG, HR, CY, CZ, EE, FR, DE, EL, HU, IT, LT, LV, MT, NL, PL, PT, RO, ES, SI, SK]
Frontline Tri-Act 135.2 mg / 1009.6 mg spot-on solution for dogs 10-20 kg
Frontline Tri-Act 270.4 mg / 2019.2 mg spot-on solution for dogs 20-40 kg
Frontline Tri-Act 405.6 mg / 3028.8 mg spot-on solution for dogs 40-60 kg

[BE, LU]
Frontect 135.2 mg / 1009.6 mg spot-on solution for dogs 10-20 kg
Frontect 270.4 mg / 2019.2 mg spot-on solution for dogs 20-40 kg
Frontect 405.6 mg / 3028.8 mg spot-on solution for dogs 40-60 kg

2. Composition

Active substances:
Each 2 ml pipette contains:
Fipronil ..... 135.2 mg
Permethrin ..... 1 009.6 mg

Each 4 ml pipette contains:
Fipronil ..... 270.4 mg
Permethrin ..... 2 019.2 mg

Each 6 ml pipette contains:
Fipronil ..... 405.6 mg
Permethrin ..... 3 028.8 mg

Excipients:
Each 2 ml pipette contains:
Butylhydroxytoluene (E321) ..... 2.250 mg
N-methylpyrrolidone ..... 787.4 mg

Each 4 ml pipette contains:
Butylhydroxytoluene (E321) ..... 4.500 mg
N-methylpyrrolidone ..... 1 574.8 mg

Each 6 ml pipette contains:
Butylhydroxytoluene (E321) ..... 6.750 mg
N-methylpyrrolidone ..... 2 362.2 mg

Clear colourless to yellow-brown spot-on solution.

3. Target species

Dogs.

4. Indications for use

For the treatment and prevention of flea and/or tick infestations where repellent (anti-feeding) activity is necessary against sandflies, biting flies and/or mosquitoes.

- Fleas

Treatment and prevention of *Ctenocephalides felis* flea infestations and prevention of *Ctenocephalides canis* flea infestations. One treatment prevents new flea infestations for 4 weeks. The product can be used as part of a treatment strategy for flea allergy dermatitis where this has been previously diagnosed by a veterinarian.

- Ticks

Treatment and prevention of tick infestations (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus*). One treatment kills (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus*) and repels (*Ixodes ricinus, Rhipicephalus sanguineus)* ticks for 4 weeks after treatment, and repels *Dermacentor reticulatus* from 7 days up to 4 weeks after treatment.

- Mosquitoes and sandflies

Repels (anti-feeding activity) sandflies (*Phlebotomus perniciosus*) for 3 weeks and mosquitoes *(Culex pipiens, Aedes albopictus*) for 4 weeks.
Kills sandflies (*Phlebotomus perniciosus)* and mosquitoes *(Aedes albopictus)* for 3 weeks.
Reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*) for up to 4 weeks. The effect is indirect due to product's activity against the vector.

- Stable flies

Repels (anti-feeding activity) and kills stable flies (*Stomoxys calcitrans*) for 5 weeks.

5. Contraindications

Do not use on sick or convalescent animals.
Do not use in cats or rabbits, as adverse reactions and even death could occur (see Special warnings).
Do not use in cases of hypersensitivity to the active substances or to any of the excipients (see Special warnings).

6. Special warnings

Special warnings:
Unnecessary use of antiparasitics or use deviating from the instructions given in this package leaflet may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal.
There may be an attachment of single ticks or bites by single mosquitoes or sandflies. For this reason, transmission of pathogens by these arthropods cannot be completely excluded if conditions are unfavorable. Single ticks may attach and detach within the first 24 hours after infestation and if ticks are present when the product is applied not all ticks may be killed within 48 hours after treatment.
Immediate protection against sandflies bites is not documented. For the reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*), treated dogs should be kept into a protected environment during the first 24 hours after the initial treatment application.
The product remains effective against fleas when treated animals are immersed in water occasionally (e.g., swimming, bathing). However, dogs should not be allowed to swim or be shampooed within 48 hours after treatment. Avoid frequent swimming and shampooing of treated dogs as this may adversely affect maintenance of product effectiveness.
The possibility that other animals in the same household can be a source of re-infestation with fleas and/or ticks should be considered, and these should be treated as necessary with an appropriate product. To aid further in reducing environmental challenge, the additional use of a suitable environmental treatment against adult fleas and their developmental stages could be recommended.

Special precautions for safe use in the target species:
In the absence of specific studies, the use of the product is not recommended in dogs younger than 8 weeks of age, or in dogs weighing less than 2 kg.
Care should be taken to avoid contact of the product with the dog's eyes.
It is important to make sure that the product is applied to an area where the animal cannot lick it off and to make sure that other animals do not lick the treatment sites following application.
Due to the presence of permethrin, the product can induce potentially fatal convulsions in cats. In case of accidental dermal (skin) exposure, wash the cat with shampoo or soap, and seek veterinary advice rapidly. To prevent cats from being accidentally exposed to the product, keep treated dogs away from cats until the application site is dry. It is important to ensure that cats do not groom the site of application on a dog which has been treated with this product. In case of exposure of this type seek veterinary advice immediately.
Do not use in cats and rabbits.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
For animal treatment only.
This product can cause skin and eye irritation. Therefore, avoid contact of the product with skin and eyes. Do not open the pipette near or towards the face. In case of ocular (eye) exposure or if eyes become irritated during administration, immediately flush the eyes with plenty of water.
If ocular (eye) irritation persists, seek medical attention. In case of dermal (skin) exposure or if skin becomes irritated during administration, immediately wash the skin with plenty of soap and water. If skin irritation persists or recurs, seek medical attention.
People with known hypersensitivity to fipronil and/or permethrin should avoid contact with the product.
The product is harmful if swallowed. Avoid hand-to-mouth contact. Do not smoke, drink or eat during application. Wash hands after use. If swallowed rinse mouth and seek medical attention if you feel unwell.
Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic (toxicity to the foetus) effects. The veterinary medicinal product should not be administered by pregnant women and women suspected of being pregnant. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product by women of childbearing age.
Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.
Keep the stored pipettes in the original blister and once used, the empty pipette should immediately be disposed of appropriately, preventing further access.

Special precautions for the protection of the environment:
The product may adversely affect aquatic organisms. Treated dogs should not be allowed to enter surface water for 2 days after treatment.

Fertility, pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in dogs during pregnancy and lactation or in animals intended for breeding. Use only according to the benefit/risk assessment by the responsible veterinarian.
Laboratory studies using fipronil or permethrin have not produced any evidence of teratogenic (capable of causing embryonic or foetal malformation) or embryotoxic (capable of causing toxicity to the embryo) effects.
Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic (toxicity to the foetus) effects.

Overdose:
Safety has been assessed with up to 5 times the maximum dose in healthy adult dogs and in puppies. Transient side-effects such as mild nervous signs, vomiting and diarrhea may occur but are resolved without treatment within 1-2 days.
Animals should always be treated with the correct pipette size according to bodyweight.
The risk of experiencing adverse events may increase with overdosing, so animals should always be treated with the correct pipette size according to bodyweight.

7. Adverse events

Dogs:

Very rare (<1 animal / 10 000 animals treated, including isolated reports):
Application site reactions[1] (skin discolouration, hair loss, itching, reddening).
Generalised itching, general hair loss, erythema (reddening).
Hyperaesthesia[2] (hypersensitivity), muscle tremor[2], ataxia[2] (loss of coordination) and other neurological signs[2].
Hyperactivity[2].
Depression[2], anorexia (not eating).
Vomiting, hypersalivation.

[1] Transient.
[2] Reversible.

If licking of the application site occurs, transient hypersalivation and vomiting may be observed.

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 topical application to the skin (spot-on use).
The minimum dose is 6.76 mg/kg bw of fipronil and 50.48 mg/kg bw of permethrin corresponding to one pipette of 2 ml per dog (weighing over 10 and up to 20 kg), one pipette of 4 ml per dog (weighing over 20 and up to 40 kg) or one pipette of 6 ml per dog (weighing over 40 and up to 60 kg).
Treatment schedule:
The use of the product should be based on a confirmed infestation or risk of infestation with fleas and/or ticks when repellent (anti-feeding) activity is also necessary against sandflies and/or mosquitoes and/or biting flies.
Depending on the ectoparasite challenge, repetition of the treatment might be indicated. In such instances, the interval between two treatments should be at least 4 weeks. For infestations with fleas and/or ticks, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

9. Advice on correct administration

To ensure a correct dosage, body weight should be determined as accurately as possible. The veterinary medicinal product is available in five sizes, corresponding to dogs weighing 2-5 kg, 5-10 kg, 10-20 kg, 20-40 kg and 40-60 kg. Select the appropriate pipette size for the weight of the dog. For

dogs over 60 kg, use the appropriate combination of two pipette sizes that most closely matches the bodyweight. Underdosing could result in ineffective use and may favour resistance development.

The product should be applied in two out-of-reach spots so that the dog cannot lick the application site. These sites are at the base of the neck in front of the shoulder blades and the middle of the neck between the base of the skull and the shoulder blades.
Remove the blister card from the package and separate one blister. Remove the pipette by cutting along the dotted line with a pair of scissors or tearing open after folding the marked corner. Holding the pipette upright away from face and body, cut the pipette tip with scissors to open. Part the coat on the back of the dog until the skin is visible. Place the tip of the pipette on the skin. Squeeze the pipette, applying about half of the content halfway down the neck between the base of the skull and the shoulder blades. Repeat the application at the base of the neck in front of the shoulder blades to empty the pipette. For best results, ensure that the product is applied directly to the skin rather than on the hair.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store in the original blister.
Do not store above 25°C.

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

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
This veterinary medicinal product should not enter water courses as fipronil/permethrin may be dangerous for fish and other aquatic organisms.

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

AT, BG, DE, ES, HR, HU, CZ, EE, FR, IT, LV, LT, MT, NL, PL, PT, RO, SK, SL: Veterinary medicinal product not subject to prescription.
BE, LU, EL, CY: Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

To be completed nationally.

Plastic card of 1 pipette containing 0.5 ml, 1 ml, 2 ml, 4 ml or 6 ml.
Carton box of 3 or 6 pipettes containing 0.5 ml, 1 ml, 2 ml, 4 ml or 6 ml each.

One size only per box.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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 and contact details to report suspected adverse reaction:
To be completed nationally.

Manufacturer for the batch release:
Boehringer Ingelheim Animal Health France SCS
4, Chemin du Calquet
31000 Toulouse
France

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

17. Other information

Fipronil is an insecticide and acaricide belonging to the phenylpyrazole family.
Permethrin belongs to the Type I class of pyrethroids, which are acaricides and insecticides with repellent activity. Permethrin in the product provides repellent activity against sandflies (*Phlebotomus perniciosus*, > 90% for 3 weeks and > 80% for an additional week), mosquitoes (*Culex pipiens, Aedes albopictus*) and ticks (*Ixodes ricinus, Dermacentor reticulatus, Rhipicephalus sanguineus*).
The product kills new infesting fleas (*C. felis, C. canis*) and ticks (*I. ricinus, R. sanguineus*) within 6 hours for a full month from 2 days after product application. The product kills fleas before they can lay eggs, preventing dog's environment contamination. In case of pre-existing infestation (*C. felis*), the product will take 24 hours to effectively start to disrupt the flea life cycle.
In one experimental study, the product was shown to indirectly reduce the risk of transmission of *Babesia canis* from infected *Dermacentor reticulatus* ticks from 7 days after application up to 4 weeks, thereby reducing the risk of canine babesiosis in treated dogs in this study.
In one experimental study, the product was shown to indirectly reduce the risk of transmission of *Ehrlichia canis* from infected *Rhipicephalus sanguineus* ticks, from 7 days after application up to 4 weeks, thereby reducing the risk of ehrlichiosis in treated dogs in this study.
However, the effectiveness of the product at reducing the transmission of these infectious agents following natural exposure under field conditions has not been investigated.
In one preliminary and one pivotal clinical field studies in an endemic area, the product applied every 4 weeks was shown to indirectly reduce the risk of transmission of *Leishmania infantum* from infected sandflies, thereby reducing the risk of canine leishmaniosis in treated dogs in these studies.

PACKAGE LEAFLET
(Plastic card of 1 pipette)

1. Name of the veterinary medicinal product

Frontline Tri-Act 405.6 mg / 3028.8 mg spot-on solution for dogs 40-60 kg [AT, BG, HR, CY, CZ, EE, FR, DE, EL, HU, IT, LT, LV, MT, NL, PL, PT, RO, ES, SI, SK]
Frontect 405.6 mg / 3028.8 mg spot-on solution for dogs 40-60 kg [BE, LU]

2. Composition

Each 6 ml pipette contains:

Active substances:
Fipronil ..... 405.6 mg
Permethrin ..... 3 028.8 mg

Excipients:
Butylhydroxytoluene (E321) ..... 6.750 mg
N-methylpyrrolidone ..... 2 362.2 mg

Clear colourless to yellow-brown spot-on solution.

3. Target species

Dogs.

4. Indications for use

For the treatment and prevention of flea and/or tick infestations where repellent (anti-feeding) activity is necessary against sandflies, biting flies and/or mosquitoes.

- Fleas

Treatment and prevention of *Ctenocephalides felis* flea infestations and prevention of *Ctenocephalides canis* flea infestations. One treatment prevents new flea infestations for 4 weeks. The product can be used as part of a treatment strategy for flea allergy dermatitis where this has been previously diagnosed by a veterinarian.

- Ticks

Treatment and prevention of tick infestations (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus*). One treatment kills (*Dermacentor reticulatus, Ixodes ricinus, Rhipicephalus sanguineus*) and repels (*Ixodes ricinus, Rhipicephalus sanguineus)* ticks for 4 weeks after treatment, and repels *Dermacentor reticulatus* from 7 days up to 4 weeks after treatment.

- Mosquitoes and sandflies

Repels (anti-feeding activity) sandflies (*Phlebotomus perniciosus*) for 3 weeks and mosquitoes *(Culex pipiens, Aedes albopictus)* for 4 weeks.
Kills sandflies (*Phlebotomus perniciosus)* and mosquitoes *(Aedes albopictus)* for 3 weeks.
Reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*) for up to 4 weeks. The effect is indirect due to product's activity against the vector.

- Stable flies

Repels (anti-feeding activity) and kills stable flies (*Stomoxys calcitrans*) for 5 weeks.

5. Contraindications

Do not use on sick or convalescent animals.
Do not use in cats or rabbits, as adverse reactions and even death could occur (see Special warnings).
Do not use in cases of hypersensitivity to the active substances or to any of the excipients (see Special warnings).

6. Special warnings

Special warnings:
Unnecessary use of antiparasitics or use deviating from the instructions given in this package leaflet may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal.
There may be an attachment of single ticks or bites by single mosquitoes or sandflies. For this reason, transmission of pathogens by these arthropods cannot be completely excluded if conditions are unfavorable. Single ticks may attach and detach within the first 24 hours after infestation and if ticks are present when the product is applied not all ticks may be killed within 48 hours after treatment. Immediate protection against sandflies bites is not documented. For the reduction of the risk of infection with *Leishmania infantum* via transmission by sandflies (*Phlebotomus perniciosus*), treated dogs should be kept into a protected environment during the first 24 hours after the initial treatment application.
The product remains effective against fleas when treated animals are immersed in water occasionally *(e.g.,* swimming, bathing). However, dogs should not be allowed to swim or be shampooed within 48 hours after treatment. Avoid frequent swimming or shampooing of treated dogs as this may adversely affect maintenance of product effectiveness.
The possibility that other animals in the same household can be a source of re-infestation with fleas and/or ticks should be considered, and these should be treated as necessary with an appropriate product. To aid further in reducing environmental challenge, the additional use of a suitable environmental treatment against adult fleas and their developmental stages could be recommended.

Special precautions for safe use in the target species:
In the absence of specific studies, the use of the product is not recommended in dogs younger than 8 weeks of age, or in dogs weighing less than 2 kg.
Care should be taken to avoid contact of the product with the dog's eyes.
It is important to make sure that the product is applied to an area where the animal cannot lick it off and to make sure that other animals do not lick the treatment sites following application.

Due to the presence of permethrin, the product can induce potentially fatal convulsions in cats. In case of accidental dermal (skin) exposure, wash the cat with shampoo or soap, and seek veterinary advice rapidly. To prevent cats from being accidentally exposed to the product, keep treated dogs away from cats until the application site is dry. It is important to ensure that cats do not groom the site of application on a dog which has been treated with this product. In case of exposure of this type seek veterinary advice immediately.
Do not use in cats and rabbits.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
For animal treatment only.
This product can cause skin and eye irritation. Therefore, avoid contact of the product with skin and eyes. Do not open the pipette near or towards the face. In case of ocular (eye) exposure or if eyes become irritated during administration, immediately flush the eyes with plenty of water.

If ocular (eye) irritation persists, seek medical attention. In case of dermal (skin) exposure or if skin becomes irritated during administration, immediately wash the skin with plenty of soap and water. If skin irritation persists or recurs, seek medical attention.
People with known hypersensitivity to fipronil and/or permethrin should avoid contact with the product.
The product is harmful if swallowed. Avoid hand-to-mouth contact. Do not smoke, drink or eat during application. Wash hands after use. If swallowed rinse mouth and seek medical attention if you feel unwell.
Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic (toxicity to the foetus) effects. The veterinary medicinal product should not be administered by pregnant women and women suspected of being pregnant. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product by women of childbearing age.
Treated animals should not be handled until the application site is dry, and children should not be allowed to play with treated animals until the application site is dry. It is therefore recommended that animals are not treated during the day, but should be treated during the early evening, and that recently treated animals are not allowed to sleep with owners, especially children.

Keep the stored pipettes in the original blister and once used, the empty pipette should immediately be disposed of appropriately, preventing further access.

Special precautions for the protection of the environment:
The product may adversely affect aquatic organisms. Treated dogs should not be allowed to enter surface water for 2 days after treatment.

Fertility, pregnancy and lactation:
The safety of the veterinary medicinal product has not been established in dogs during pregnancy and lactation or in animals intended for breeding.
Use only according to the benefit/risk assessment by the responsible veterinarian.

Laboratory studies using fipronil or permethrin have not produced any evidence of teratogenic (capable of causing embryonic or foetal malformation) or embryotoxic (capable of causing toxicity to the embryo) effects.
Laboratory studies in rabbits and rats with the excipient N-methyl pyrrolidone have shown evidence of foetotoxic (toxicity to the foetus) effects.

Overdose:
Safety has been assessed with up to 5 times the maximum dose in healthy adult dogs and in puppies. Transient side-effects such as mild nervous signs, vomiting and diarrhea may occur but are resolved without treatment within 1-2 days.
Animals should always be treated with the correct pipette size according to bodyweight.

The risk of experiencing adverse events may increase with overdosing, so animals should always be treated with the correct pipette size according to bodyweight.

7. Adverse events

Dogs:

Very rare (<1 animal / 10 000 animals treated, including isolated reports):
Application site reactions[1] (skin discolouration, hair loss, itching, reddening).
Generalised itching, general hair loss, erythema (reddening).
Hyperaesthesia[2] (hypersensitivity), muscle tremor[2], ataxia[2] (loss of coordination) and other neurological signs[2].
Hyperactivity[2].
Depression[2], anorexia (not eating).

Vomiting, hypersalivation.

[1] Transient.
[2] Reversible.

If licking of the application site occurs, transient hypersalivation and vomiting may be observed.

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 topical application to the skin (spot-on use).
The minimum dose is 6.76 mg/kg bw of fipronil and 50.48 mg/kg bw of permethrin corresponding to one pipette of 6 ml per dog (weighing over 40 and up to 60 kg).

Treatment schedule:
The use of the product should be based on a confirmed infestation or risk of infestation with fleas and/or ticks when repellent (anti-feeding) activity is also necessary against sandflies and/or mosquitoes and/or biting flies.
Depending on the ectoparasite challenge, repetition of the treatment might be indicated. In such instances, the interval between two treatments should be at least 4 weeks. For infestations with fleas and/or ticks, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

9. Advice on correct administration

To ensure a correct dosage, body weight should be determined as accurately as possible. The veterinary medicinal product is available in five sizes, corresponding to dogs weighing 2-5 kg, 5-10 kg, 10-20 kg, 20-40 kg and 40-60 kg. Select the appropriate pipette size(s) for the weight of the dog. For dogs over 60 kg, use the appropriate combination of two pipette sizes that most closely matches the bodyweight. Underdosing could result in ineffective use and may favour resistance development.

The product should be applied in two out-of-reach spots so that the dog cannot lick the application site. These sites are at the base of the neck in front of the shoulder blades and the middle of the neck between the base of the skull and the shoulder blades.
Remove the blister card from the package and separate one blister. Remove the pipette by cutting along the dotted line with a pair of scissors or tearing open after folding the marked corner. Holding the pipette upright away from face and body, cut the pipette tip with scissors to open. Part the coat on the back of the dog until the skin is visible. Place the tip of the pipette on the skin. Squeeze the pipette, applying about half of the content halfway down the neck between the base of the skull and the shoulder blades. Repeat the application at the base of the neck in front of the shoulder blades to empty the pipette. For best results, ensure that the product is applied directly to the skin rather than on the hair.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store in the original blister.
Do not store above 25°C.

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

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
This veterinary medicinal product should not enter water courses as fipronil/permethrin may be dangerous for fish and other aquatic organisms.

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

AT, BG, DE, ES, HR, HU, CZ, EE, FR, IT, LV, LT, MT, NL, PL, PT, RO, SK, SL: Veterinary medicinal product not subject to prescription.
BE, LU, EL, CY: Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

To be completed nationally.

Plastic card of 1 pipette containing 0.5 ml, 1 ml, 2 ml, 4 ml or 6 ml.
Carton box of 3 or 6 pipettes containing 0.5 ml, 1 ml, 2 ml, 4 ml or 6 ml each.
One size only per box.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}

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 and contact details to report suspected adverse reaction:
To be completed nationally.

Manufacturer for the batch release:
Boehringer Ingelheim Animal Health France SCS
4, Chemin du Calquet

31000 Toulouse
France

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

17. Other information

Fipronil is an insecticide and acaricide belonging to the phenylpyrazole family.
Permethrin belongs to the Type I class of pyrethroids, which are acaricides and insecticides with repellent activity. Permethrin in the product provides repellent activity against sandflies (*Phlebotomus perniciosus*, > 90% for 3 weeks and > 80% for an additional week), mosquitoes (*Culex pipiens, Aedes albopictus*) and ticks (*Ixodes ricinus, Dermacentor reticulatus, Rhipicephalus sanguineus*).
The product kills new infesting fleas (*C. felis, C. canis*) and ticks (*I. ricinus, R. sanguineus*) within 6 hours for a full month from 2 days after product application. The product kills fleas before they can lay eggs, preventing dog's environment contamination. In case of pre-existing infestation (*C. felis*), the product will take 24 hours to effectively start to disrupt the flea life cycle.
In one experimental study, the product was shown to indirectly reduce the risk of transmission of *Babesia canis* from infected *Dermacentor reticulatus* ticks from 7 days after application up to 4 weeks, thereby reducing the risk of canine babesiosis in treated dogs in this study.
In one experimental study, the product was shown to indirectly reduce the risk of transmission of *Ehrlichia canis* from infected *Rhipicephalus sanguineus* ticks, from 7 days after application up to 4 weeks, thereby reducing the risk of ehrlichiosis in treated dogs in this study.
However, the effectiveness of the product at reducing the transmission of these infectious agents following natural exposure under field conditions has not been investigated.
In one preliminary and one pivotal clinical field studies in an endemic area, the product applied every 4 weeks was shown to indirectly reduce the risk of transmission of *Leishmania infantum* from infected sandflies, thereby reducing the risk of canine leishmaniosis in treated dogs in these studies.