SHOTWELL & CARR, INC. SERVING THE FDA/EPA/USDA REGULATED INDUSTRIES SINCE 1974

1415 HALSEY WAY, SUITE 304, CARROLLTON, TX 75007-4455
PHONE (972) 446-6611 TOLL FREE (888) 326-3311 FAX (972) 446-6622
E-MAIL: pwcarr@shotcarr.com
Web Page: www.shotcarr.com

April 19, 2013

Dockets Management Branch
Food and Drug Administration
Room 1061 (HFA-305)
5630 Fishers Lane
Rockville, MD 20852

Re: Suitability Petition – Cyclosporine oral solution for dogs

Dear Sir or Madam,

The undersigned submits this petition under the provisions of Section 512(n)(3) of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of the Food Drug Administration (FDA) make a determination that a new dosage form of generic oral cyclosporine that differs from the reference product (ATOPICA® (Cyclosporine) NADA # 141-218) is suitable for filing under an abbreviated new animal drug application (ANADA).

1. Action requested

Petitioner request the FDA make a determination that a new dosage form of cyclosporine oral solution for dogs (proposed trade name Cyclosporine 100 mg/mL Oral Solution) is suitable for submission as an ANADA. Petitioner's proposed product differs from the reference product, (ATOPICA® (cyclosporine) NADA # 141-218), in the following way:

Reference product

Trade name: ATOPICA® (NADA # 141-218)

Active ingredient: Cyclosporine

Dosage form: Gelatin capsules

Strength: 10, 25, 50 and 100 mg capsules (10% w/w cyclosporine)

Sponsor: Novartis Animal Health US

Route of administration: oral

Dosage/ Direction for use: 5 mg/kg/day (3.3-6.7 mg/kg/day) as a single daily dose for 30 days.

Dog body weight (lbs)	Dog body weight (kg)	Dose 5 mg/kg
4 – 6.5	2 – 2.9	10 mg capsule
6.6 – 9	3 – 3.9	2 x 10 mg capsules
9.1 -16	4 – 7.9	25 mg capsule
16.1 – 33	8 – 14.9	50 mg capsule
33.1 – 64	15 – 28.9	100 mg capsule
64.1 – 79	29 – 35.9	100 mg capsule + 50 mg capsule
79.1 - 121	36 – 55.9	2 x 100 mg capsules

A copy of the publicly available Freedom of Information Summary for ATOPICA (NADA # 141-218), the reference product, is presented in Appendix 1. The active ingredient and the strength of the proposed cyclosporine oral solution will be the same as the reference product. Details regarding Petitioner's proposed product are set below:

Proposed drug product

Trade name: Cyclosporine 100 mg/mL Oral Solution

Active ingredient: Cyclosporine

Dosage form: Oral solution

Strength: 10% w/w cyclosporine

Route of administration: oral

Dosage/Direction for use: 5 mg/kg/day for 30 days. The proposed product should be administered directly into the mouth using the dispensing system (graduated syringe) included in the packaging.

The drug itself, active ingredient, route of administration, strength of the solution (included in capsules of ATOPICA®) and administered dose (5 mg/kg per animal) are the same as those of the reference product and the proposed product would differ from the reference product approved under NADA # 141-218 only in dosage form.

2. Statement of Grounds

The reference drug that is the basis for this petition – ATOPICA® (cyclosporine) NADA # 141-218 – is an oral formulation of cyclosporine that immediately forms a microemulsion in an aqueous environment. This oral solution is contained within gelatin soft capsules. The reference drug contains the same active ingredient as the proposed new dosage form, but is marketed as oral gelatin capsules for administration. The change requested in this petition is a dosage form: from oral solution in gelatin capsules to a comparable oral solution without capsules.

The petitioner seeks to register a new dosage form product, an oral solution directly administered to dogs as a generic product of ATOPICA® capsules for dog.

Four presentations are available for the reference product - capsules containing 10 mg, 25 mg, 50 mg and 100 mg of cyclosporine.

Four presentations will also be available for Cyclosporine Oral Solution - 5, 15, 30 and 50 mL vials containing 100 mg/mL of cyclosporine.

An oral solution will provide veterinarians, other practitioners and owners with a convenient alternative to the currently approved dosage form. The proposed product will be formulated as an oral solution instead of capsule form in order to facilitate the administration of the product. For the cat, in which products are not easy to administer, the dispensing system using an oral syringe was chosen. For dog species administration of a solution by oral syringe will also be easier than administration of a solid form.

Moreover, calibrated syringes are used to administer the proposed product. The syringes are graduated (0.05 mL for 1 mL syringes and 0.1 mL for 2 mL syringes) and the dose administered with the oral solution is much more accurate than capsules, which are given for a range of bodyweights, and in certain conditions two capsules must be given at the same time to one animal to achieve the labeled dose.

With this new presentation of the product (oral solution), animals could then receive exactly 5 mg/kg of active ingredient.

The package insert for the reference drug product is available in Appendix 2, and labeling for the proposed drug is attached in Appendix 3.

The labeling for the proposed product is similar to that of the reference drug: "Description", "indications", "dosage and administration", "contraindications", "warnings", "precautions", "effectiveness field study", "adverse reactions", "clinical pharmacology, metabolism", "animal safety" paragraphs are fully identical between the reference product ATOPICA® and the proposed Cyclosporine 100 mg/mL Oral Solution.

The labeling will differ only with respect to the dosage administration paragraph, storage conditions, product presentations and manufacturer-specific information.

The "Dose administration" table for Cyclosporine 100 mg/mL Oral Solution is derived from the reference product table, but modified to account for the differing liquid dosage form.

The" storage conditions" wording will depend on stability study results for Cyclosporine Oral Solution.

The "how supplied" paragraphs differ between the two products to indicate the proposed product presentation, manufacturer of Cyclosporine 100 mg/mL Oral Solution and ANADA number.

3. Environmental impact

Petitioner claims a categorical exclusion from the requirement to file an environmental impact assessment under 21 C.F.R. § 25.33(d) (5) as the proposed drug product is restricted to use by or on the order of a licensed veterinarian.

To the best of Petitioner's knowledge, no extraordinary circumstances exist that may significantly affect the human environment, as discussed under 21 CFR 25.21.

4. Economic impact

An economic impact analysis will be provided if requested by the Commissioner after review of this petition.

5. Certification

To the best knowledge and belief of the undersigned, this petition includes all information and views upon which the petition relies, including representative data and information known to be unfavorable.

6. Confidential and/or Proprietary information

In accordance with applicable provisions of the Freedom of Information Act (FOIA) and 21 C.F.R. § 20.61, Petitioner submits that no information contained within this petition constitutes privileged or confidential trade secrets and/or commercial or financial information exempt from disclosure under exemption 4 of the Freedom of Information Act.

Please address all correspondence relating to this matter to the undersigned.

Sincerely,

Paul W Carr

Paul W. Carr. P.E., R.A.C.
President