SCIENTIFIC DISCUSSION

1. SUMMARY OF THE DOSSIER

Rheumocam is a generic medicinal product as defined in Article 13(2) (b) of Directive 2001/82/EC, as amended by Directive 2004/28/EC. The reference veterinary medicinal product is Metacam 1.5 mg/ml oral suspension for dogs, a product with a Community Marketing Authorisation and originally authorised in Germany in 1992.

The active substance is meloxicam, a non-steroidal anti-inflammatory drug belonging to the acidic enolcarboxamide (oxicam) class. *In vitro* meloxicam is preferentially active against cyclooxygenase-2. The recommended posology consists of an initial single dose of 0.2 mg meloxicam/kg body weight on the first day, followed by once daily administration (24-hour intervals) of 0.1 mg meloxicam/kg body weight. The product is to be administered mixed with food.

According to the legislation, it is not required to provide the results of the safety and residue tests or of the pre-clinical and clinical trials once it is demonstrated that the medicinal product is a generic of a reference medicinal product for which the data exclusivity period has expired.

According to Article 13(2) (b) of Directive 2001/82/EC, as amended by Directive 2004/28/EC, a generic medicinal product is defined as having the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies. The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information intended to provide proof of the safety and/or efficacy of the various salts, esters or derivatives of an authorised active substance must be supplied. The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form. Bioavailability studies need not be required if it is demonstrated that the generic medicinal product meets the relevant criteria as defined in the appropriate detailed guidelines.

The company submitted an application to the EMEA on 28 October 2008 for the granting of an extension to the Community marketing authorisation for Rheumocam to include 1 mg and 2.5 mg chewable tablets in accordance with Annex II of Reg. 1084/2003 of 3 June 2003.

2. QUALITY ASSESSMENT

Composition of the Veterinary Medicinal Product

Rheumocam oral suspension for dogs contains 1.5 mg/ml meloxicam as active substance. Conventional pharmaceutical excipients are used and full details are included in the Summary of Product Characteristics (SPC). The primary packaging materials consist of a white polyethylene bottle with a polypropylene measuring syringe and tamper proof child resistant closure. Pack sizes are 42 ml, 100 ml or 200 ml.

Rheumocam chewable tablets contain 1 mg and 2.5 mg meloxicam respectively as active substance and are packed in blister packs made up of a PVC/PVDC (250.60) with a 20µm foil (Al foil). Pack sizes are of 20 and 100 tablets.

Development Pharmaceutics

Rheumocam has been formulated to be essentially similar to the reference product, Metacam oral suspension 1.5 mg/ml, and contains the same active ingredient, meloxicam, used in the reference

product. Rheumocam oral suspension has comparable physical characteristics to the reference Metacam product, i.e. viscosity and pH.

Meloxicam is a stable substance and no interactions with the excipients have been observed. The excipients used in this formulation are well known and commonly used in the pharmaceutical and food industry. Sodium carboxymethyl cellulose and colloidal silicon dioxide are widely used as suspending agents in oral suspensions. The pharmacokinetics of the test product, Rheumocam Oral Suspension and the reference product, Metacam Oral Suspension, were compared in the target species dogs, by way of a bioequivalence study. The results of the bioequivalence study show that the products are bioequivalent within normal confidence limits established in the Guideline (EMEA/CVMP/016/00) for the Conduct of the Bioequivalence Study for Veterinary Medicinal Products.

Sodium benzoate has been chosen as a suitable preservative as it is effective against bacteria and moulds in low concentration, has low toxicity and is stable and active over a wide range of pH and temperatures. Sodium benzoate is also used as the preservative in the reference product Metacam 1.5 mg/ml. Preservative efficacy testing was performed at the initial time point for the stability batches and the results conformed to the European Pharmacopoeia (Ph.Eur.) acceptance criteria A. 5.1.3.

As sweeteners sorbitol solution and sodium saccharin have been chosen as they are widely used in suspensions. Disodium hydrogen phosphate dodecahydrate and citric acid monohydrate have been chosen as buffering agents. The levels have been chosen to give a pH value similar to that of Metacam 1.5 mg/ml.

Rheumocam 1.5 mg/ml oral suspension is packed in polyethylene bottles with a polypropylene measuring syringe and a polyethylene tamper proof child resistant closure. The suitability of the primary packaging was investigated as part of the stability studies performed.

For Rheumocam chewable tablets the formulation has been developed to be bioequivalent to the reference product; Metacam tablets and contains the same active ingredient used in the reference product. Meloxicam, the active ingredient, is purchased to British Pharmacopoeia (BP) specification with a Certificate of Analysis detailing the tests conducted by the manufacturer. During the procedure the applicant confirmed that the meloxicam had been updated to Ph.Eur. specification. Each of the excipients with the exception of the flavouring agent is purchased to Ph.Eur specifications. The properties of the excipients are well known and are used frequently in the solid dosage forms. The only exception in this case is flavouring, i.e. Pork Flavour Givaudan which conforms to the supplier's internal standards.

Method of manufacture

Oral suspension

Manufacturing Formula and Batch Size

The proposed batch sizes range for the manufacture of Rheumocam 1.5mg/ml oral suspension were defined and the manufacturing formula for the standard batch size was provided. For larger batch sizes, quantities and volumes are scaled up accordingly.

Manufacturing Process and In-process Controls

A flow diagram of the manufacturing process for the standard batch size was provided and details of the in-process controls performed were also provided. The manufacturing process and in-process controls are described appropriately and are considered adequate.

Validation of Manufacturing Process

A validation study has been performed on the first full scale manufacturing batches produced in stainless steel tanks. All results were within the acceptance criteria set up in the validation report.

Chewable tablets

Manufacturing Formula and Batch Size

The proposed commercial batch sizes range for the manufacture of Rheumocam 1 mg and 2.5 mg tablets were defined for each tablet strength and the manufacturing formula presented.

Manufacturing Process and In-process Controls

A flow diagram of the manufacturing process for the standard batch size was provided and details of the in-process controls performed were also provided. The manufacturing process and in-process controls are described appropriately and are considered adequate.

Validation of Manufacturing Process

Validation reports for the tabletting mixture preparation (blend) and compressing procedure for a number of batches for 1mg and 2.5mg Rheumocam tablets were presented. Data from validation studies confirmed that the manufacturing process for Rheumocam tablets (2.5mg and 1mg) using materials of the stated quality and the equipment specified is a suitable one and will consistently yield the product of the desired quality as described in the Finished Product Specifications.

CONTROL OF STARTING MATERIALS

Active Substance: Specification and routine tests

Meloxicam (BP), updated during procedure to Ph.Eur.

A Drug Master File (DMF) for the active substance manufacturer was provided with all relevant data and complying with the BP monograph for the raw material. Additional in-house tests were also described.

Analytical methods and validation

The assay of meloxicam is by non-aqueous titration and related substances are determined by the methods described in the British Pharmacopoeia monograph. Additional in-house methods were also described and these methods have been validated.

Physico-Chemical Characteristics liable to affect bioavailability

Meloxicam exists in 5 polymorphic forms I, II, III, IV and V. These forms can be differentiated on the basis of their Infrared absorption spectra and X-Ray diffraction pattern. The active substance supplier routinely manufactures polymorphic form I for supply to the applicant for the manufacture of meloxicam liquid. Particle size was limited on the active substance specification.

Scientific data

Nomenclature

Nomenclature of the active substance is presented:

Generic name:	Meloxicam (INN, BAN)
Chemical name:	4-hydroxy-2-methyl-N-(5-methyl-1,3-thiazol-2-yl)-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide
CAS No.:	71125-38-7

Description

Description of the active substance: pale yellow powder
Molecular formula: $C_{14}H_{13}O_4N_3S_2$
Molecular weight: 351.4

Quality control during manufacture

Appropriate quality control is carried out.

Development chemistry

The development chemistry was presented.

Evidence of structure

The chemical structure has been confirmed by: elemental analysis, mass spectrum, ^{1}H-NMR, ^{13}C-NMR, HPLC, IR and UV. Examples of spectra were provided. All tests showed that the structure of the substance corresponds to the structure of meloxicam.

Physico-chemical characterisation

The solubility is described in the British Pharmacopoeia monograph. No literature describes isomerism for meloxicam. From literature it is known that meloxicam shows polymorphism with two different crystalline forms known: the zwiterionic form (referred to form IV) and the enolic form (form I). The differences of the two forms are controlled by IR. British Pharmacopoeia IR is form I and the active substance supplier product is form I. Various validated analytical methods for release of finished product are used.

Impurities

Meloxicam is tested in accordance with the British Pharmacopoeia. Potential known impurities were identified.

Residual solvents

Residual solvents used in the manufacturing process of meloxicam were listed which are limited on the specification in line with EU/VICH limits.

Batch analysis

Satisfactory data on batch results were presented and all results were within the relevant specifications.

Excipients

Oral suspension

Excipients described in a Pharmacopoeia

All excipients are tested according to their corresponding monographs except for honey flavour, which is tested according to the supplier's specifications. The relevant certificates of analysis issued by the suppliers have been provided. All excipients comply with their respective monographs and typical certificates of analysis demonstrating compliance for each are provided.

Excipient not described in a Pharmacopoeia

Honey flavour is not described in a pharmacopoeia. The certificate of analysis issued by the supplier and details of the in-house tests and specifications have been provided. The main constituent of honey flavour is a well-established pharmaceutical formulation excipient. The technical data sheet for honey flavour also states that this excipient is recommended for general pharmaceutical applications. The stability data provided demonstrate that the excipient honey flavour is compatible with both the active ingredient meloxicam and with the other excipients present in Rheumocam 1.5 mg/ml Oral Suspension.

Chewable tablets

Excipients described in a Pharmacopoeia

All excipients are tested according to their corresponding monographs except for Pork Flavour, which is tested according to the supplier's specifications. The relevant certificates of analysis issued by the suppliers have been provided.

Excipient not described in a Pharmacopoeia

Pork Flavour is not described in a pharmacopoeia. The relevant certificate of analysis issued by the supplier has been provided.

Packaging Material

Oral suspension

The primary packaging materials consist of a white polyethylene terephthalate (PET) bottle closed with a child proof tamper evident high density polyethylene cap. The temper evident ring is high density polyethylene coloured to the yellow colour, the input of the cap is made from low density polyethylene. PET complies with the requirements of the European Community and National Food Packaging Regulations. As well as a declaration from the supplier certifying that PET resins comply with the Ph. Eur. 4th edition 3.1.15 ("Polyethylene terephthalate for containers for preparations not for parental use"), it was confirmed that the PET conforms with the requirements from Ph. Eur. and specifications for tamper evident lids used in the initial stability studies and stability studies were provided. Stability studies performed in the final packaging have been addressed and no incompatibilities between the immediate packaging and suspension have been found.

Chewable tablets

The primary packaging material consists of PVC/PVDC with a 20µm foil. Certificates from the manufacturers were provided. Some routine tests for foils of blisters include: correct dimension, appearance, correct code number, correct grade material, pin hole test, heat sealing, IR identification. Stability studies performed in the final packaging show that no incompatibilities between the immediate packaging and tablets have been found.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

Declarations were provided from all manufacturers of the starting materials that no input materials used for the production of the finished product fall within the scope of the guidance "Note for guidance on minimising the risk of Transmitting animal Spongiform Encephalopathy agents via Human and Veterinary Medicinal Products" (EMEA/410/01-Rev.2).

Control Tests On Finished Product

Product Specification and Routine Tests

Oral suspension

The finished product release and shelf life specifications were provided.

Chewable tablets

The specification complies in general with VICH requirements and Acceptance Criteria for New Veterinary Drug Substances and New Medicinal Products: Chemical Substances and meets the requirements of the general method of the European Pharmacopoeia for "Tablets" (Dosage Forms). Methods used for identification and assay of meloxicam were described. Details for the meloxicam quantification during the dissolution tests of Rheumocam Tablets (1 mg and 2.5 mg strength) have been provided also.

Scientific Data

Analytical validation of methods and comments on the choice of routine tests and standards

Oral suspension

The methods used for identification and assay of meloxicam and to determine sodium benzoate were provided. The methods have been fully validated and the validation reports were provided.

Chewable tablets

Assay validation for content of meloxicam in Rheumocam tablets was detailed. The assay was validated according to current VICH requirements; validation of analytical procedures. The parameters evaluated during the validation of the assay with the acceptance criteria were described. The assay for determination of the concentration of meloxicam after dissolution of Rheumocam tablets has been described and validated. The assay was validated according to current VICH requirements: Validation of analytical procedures.

Batch analyses

Batch analyses of production batches for both the oral suspension and chewable tablets manufactured at Chanelle Pharmaceuticals Manufacturing Ltd., Ireland were presented. The results conformed to the relevant specifications.

Stability

Oral suspension

Stability Tests on the Active Substance(s)

The following re-test period/storage condition was proposed: 24 months / no special requirements for storage. The stability data support 2 years with no special storage conditions. Stability studies have been carried out on batches at 25°C/ RH 60% up to 24 months and at accelerated conditions 40 °C/ RH 75% for 6 months. All relevant parameters of the specification were investigated.

Stability Tests on the Finished Product

A description was provided of relevant stability studies performed. Stability data from batches of finished product in the package not intended for marketing (white polyethylene bottles with a tamper evident polyethylene cap) were available. The batches were stored for 24 months at 25°C/60% RH and 6 months at 40°C/75% RH. No significant changes at both conditions were observed. The results remained within specification limits. The data supported the absence of a storage precaution for the product and a shelf-life of 2 years with no specific precaution for storage was considered acceptable.

In-use Stability Tests

Stability results were presented for batches stored at 25°C 60% RH for 24 months and for batches at 40°C 75% RH for 6 months. These stability results seem to demonstrate that the product stored in a semi-permeable container can withstand low relative humidity environments. The applicant has committed to providing additional stability data to support this.

Chewable tablets

Stability Tests on the Active Substance(s)

Details on the stability of the raw material, meloxicam, were provided.

Stability Tests on the Finished Product

Stability data from a number of batches of finished product in the package were presented, having been stored for 6 months at 40°C/ 75% RH and 12 months at 25°C/ 60% RH. Observed parameters were within specification limits.

A shelf-life of 3 years is considered acceptable in light of the post-opinion commitment that the long term stability studies on the finished product are continued throughout the approved shelf-life period. The results should be available upon request and the EMEA must be informed immediately should stability problems arise during the studies

In-use Stability Tests

No data was provided. As the active substance has been shown to be stable and this also is the case for the finished product when stored in blister packs, it is considered acceptable not to perform in-use stability testing.

3. SAFETY ASSESSMENT

As essential similarity to the reference product was confirmed, the results of toxicological and pharmacological tests and clinical trials were not required in accordance with Article 13 of Directive 2001/82/EC, as amended.

Pharmacodynamics

The application was made in accordance with Article 13(1) of Directive 2001/82/EC (as amended), a generic application, and therefore data on pharmacodynamics were not required.

Toxicological studies

As essential similarity to the reference product was confirmed and in accordance with Article 13.1(a)(iii) of Directive 2001/82/EC, as amended by Directive 2004/28/EC, the toxicological profile of meloxicam does not need to be reassessed.

User Safety

A satisfactory user safety assessment has been provided by the Applicant.

Inherent Toxicity

Given that Rheumocam is demonstrated to be bioequivalent to Metacam, the potential impact of the active substance in respect of user safety will be the same for both products. The excipients used in the formulation are well established and have an extensive history of use in oral preparations at concentrations comparable to those specified for Rheumocam. Given the known use of the excipients and the expected safety profile, it is not expected that the excipients will present a hazard to either the target animal or the user.

Exposure of the user

The intended posology and indications are identical to those of the reference product, Metacam, therefore, the same exposure scenarios exist.

Risk management phrases as authorised for Metacam are included in the SPC and product literature:

- People with known hypersensitivity to NSAIDs should avoid contact with the veterinary medicinal product.
- In case of accidental self administration, seek medical advice immediately and show the package insert or the label to the physician.

Based on the fact that bioequivalence is demonstrated with Metacam, that the excipients included in the formulations can be considered safe and that the posology and indications are identical to those of the reference product, it can be accepted that the potential hazard to the user posed by Rheumocam will not be any greater than that posed by the reference product. The proposed user safety statements were considered appropriate.

Environmental Risk Assessment

Phase I Assessment

The product is intended to be used in dog, a companion animal, and the environmental risk assessment stopped in Phase I because of this.

4. EFFICACY ASSESSMENT

Oral suspension

This application was presented in accordance with Article 13(1) of Directive 2001/82/EC as amended, which refers to applications for veterinary medicinal products which are generics of a reference medicinal product authorised within the Community. In accordance with this provision, Rheumocam is a generic of Metacam 1.5 mg/ml oral suspension for dogs (Boehringer Ingelheim Vetmedica).

The active substance is meloxicam, a non-steroidal anti-inflammatory drug belonging to the acidic enolcarboxamide (oxicam) class. *In vitro* meloxicam is preferentially active against cyclooxygenase-2.

The proposed indication for Rheumocam 1.5 mg/ml Oral Suspension for Dogs is for the alleviation of inflamation and pain in both acute and chronic musculo-skeletal disorders**.**

The recommended posology consists of an initial single dose of 0.2 mg meloxicam/kg body weight on the first day, followed by once daily administration (24-hour intervals) of 0.1 mg meloxicam/kg body weight. The product is to be administered mixed with food, and measured using a measuring syringe as supplied with the product.

As essential similarity to the reference product was confirmed, the results of toxicological and pharmacological tests and clinical trials were not required in accordance with Article 13(1) of Directive 2001/82/EC, as amended. The reference and the test products have the same pharmaceutical form (oral suspension) and the reference and the test products have the same qualitative and quantitative composition in active substance: 1.5 mg/ml of meloxicam.

Pharmacokinetics

A study of bioequivalence *in vivo* was performed in dogs between the 2 formulations Rheumocam and Metacam after a single oral administration. The study was designed to meet the requirements of the Guideline for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMEA/CVMP/016/00).

Fasting Beagle dogs were treated with a single oral administration of meloxicam. Food was given immediately after the treatment.

The protocol was a two period, two treatment, two sequence crossover design. Dogs were observed several times daily for appearance and behaviour, blood samples were stored at –20°C and the sampling times were pre-dose and at appropriate time intervals post-dose. The analytical method was appropriate and was validated in a GLP study.

The pharmacokinetic parameters of meloxicam following oral administration in dogs of meloxicam were studied and in the results of the bioequivalence analysis the confidence intervals for the parameters $AUC_{0\text{-infinity}}$ and Cmax were within the acceptable range, therefore it was concluded that Rheumocam was bioequivalent to the reference product Metacam when administered to dogs. Similarities in T1/2 elim showed that there were no differences in kinetics between the two formulations.

Tolerance in the target species of animal

The active substance, meloxicam, is present in Rheumocam in the same concentration as in the reference product Metacam. In respect of active substance, a similar tolerance profile for both products can be assumed. Excipients present in the formulation of Rheumocam are commonly used in veterinary medicines and food products and can be considered safe. In view of the above, it was concluded that the safety profile of Rheumocam is comparable to Metacam and therefore the same warnings are included in the SPC and product literature, as follows:

- Do not use in pregnant or lactating animals
- The safety of the veterinary medicinal product has not been established during pregnancy and lactation
- Do not use in animals suffering from gastrointestinal disorders such as irritation and haemorrhage, impaired hepatic, cardiac or renal function and haemorrhagic disorders, or where there is evidence of individual hypersensitivity to the product.
- Do not use in dogs less than 6 weeks of age
- Typical adverse drug reactions of NSAIDs such as loss of appetite, vomiting, diarrhoea, faecal occult blood and apathy have occasionally been reported. These side effects occur generally within the first treatment week and are in most cases transient and disappear following termination of the treatment but in very rare cases may be serious or fatal.

- If side effects occur, treatment should be discontinued and the advice of a veterinarian should be sought.
- Avoid use in any dehydrated, hypovolaemic or hypotensive animal, as there is a potential risk of increased renal toxicity.
- Other NSAIDs, diuretics, anticoagulants, aminoglycoside antibiotics and substances with high protein binding may compete for binding and thus lead to toxic effects. Rheumocam must not be administered in conjunction with other NSAIDs or glucocorticosteroids.
- Pre-treatment with anti-inflammatory substances may result in additional or increased adverse effects and accordingly a treatment free period with such drugs should be observed for at least 24 hours before the commencement of treatment. The treatment-free period, however, should take into account the pharmacokinetic properties of the products used previously.

The information relating to adverse effects, precautions for use, interactions and overdose included on the proposed SPC for Rheumocam is similar to that included on the SPC of the reference product, Metacam.

Chewable tablets

Data were presented relating to a GLP study intended to demonstrate bioequivalence of Rheumocam 2.5 mg chewable tablet for dogs with the authorised reference product Metacam 2.5 mg chewable tablet for dogs. The study was designed to meet the requirements of the Guideline for the Conduct of Bioequivalence Studies for Veterinary Medicinal Products (EMEA/CVMP/016/00).

Pharmaceutical form

The test and the reference products had the same pharmaceutical form: chewable tablet.

Active substance qualitative and quantitative composition

The test and reference products had the same qualitative and quantitative composition in terms of active substances: 1 or 2.5 mg of meloxicam per chewable tablet.

Bioequivalence studies

A GLP bioequivalence study was performed in dog following single oral administration of one tablet per animal with the products Metacam 2.5 mg chewable tablet for dogs and Rheumocam 2.5 mg chewable tablet for dogs.

Based on the results of the in-life animal phase, the results of the meloxicam plasma analytical phase, the resulting derived pharmacokinetic parameters and their subsequent bioequivalence statistical analysis, it was concluded that Rheumocam 2.5 mg chewable tablet for dogs is bioequivalent to the registered reference compound Metacam 2.5 mg chewable tablet for dogs.

The bioequivalence between the 2 products Metacam and Rheumocam 2.5 mg chewable tablet for dogs was demonstrated for the main kinetic parameters: Cmax and AUCinfinity and with the additional parameter T1/2 terminal.

Comparative dissolution

A comparative dissolution was performed between Metacam 2.5 mg chewable tablet for dogs and Rheumocam 2.5 mg chewable tablet for dogs in phosphate buffer at pH 7.5 and 4.5 and in 0.1M HCl.

Another comparative dissolution was performed between Rheumocam 1 mg chewable tablet for dogs and Rheumocam 2.5 mg chewable tablet for dogs, and between Metacam 1 mg chewable tablet for dogs and Rheumocam 1 mg chewable tablet for dogs.

This application was submitted in accordance with Article 13.1 (a) (ii) of Directive 2001/EC, as amended by Directive 2004/28/EC. This provision exempts the applicant from having to provide the results of toxicological and pharmacological tests, if it can be shown that the product is essentially similar to an authorised reference product. 'Essentially similar' requires that the products contain the same active substance in the same concentration, have the same pharmaceutical form, and are bioequivalent.

Since bioequivalence has been shown, it is expected that the products in terms of efficacy and safety will behave in a very similar manner.

5. BENEFIT RISK BALANCE

Oral suspension

The application for Rheumocam 1.5 mg/ml oral suspension was a generic application. The aim of the development work was to develop an oral suspension essentially similar to the reference product Meloxicam 1.5 mg/ml oral suspension for dogs. The composition is based on the composition of the reference product. This application was submitted in accordance with Article 13.1 of Directive 2001/82/EC, as amended. Since bioequivalence was confirmed *in vivo* between the two products Rheumocam and the reference product Metacam oral suspension in dogs, Rheumocam is expected to be as safe and efficacious as Metacam oral suspension. No toxicological data have been submitted, and are not required as bioequivalence to the reference product is demonstrated.

The safety of Rheumocam to the target species and to the user has been established by:

- the bioequivalence between the two products;
- a satisfactory impurity profile of meloxicam in Rheumocam;
- the fact that a comparable safety profile was obtained with both products in the bioequivalence study.
- the excipients used in the formulation are well established and have an extensive history of use in oral preparations at concentrations comparable to those specified for Rheumocam. Given the known use of the excipients and the expected safety profile, it is not expected that the excipients will present a hazard to either the target animal or the user.
- a declaration has provided that the excipients and active ingredient are not of animal origin and that no materials of animal origin are used in the process.

Target animal and user safety warnings are the same as those for the reference product. No impact on the environment is anticipated.

Risk management statements as authorised for Metacam are included in the SPC and product literature:

- People with known hypersensitivity to NSAIDs should avoid contact with the veterinary medicinal product
- In case of accidental ingestion, seek medical advice immediately and show the package insert or the label to the physician.

Rheumocam will be used in the same way as Metacam, and thus the exposure of the user will be the same for both products and the same warnings are appropriate.

Efficacy has been established by demonstration of essential similarity to the reference product, Metacam, and by confirmation of bioequivalence between the two products when administered as recommended to the target species, dogs.

Based on the original and complementary data presented, the Committee for Medicinal Products for Veterinary Use concluded that the quality, safety and efficacy of the product were considered to be in accordance with the requirements of Directive 2001/82/EEC, as amended.

Chewable tablets

Rheumocam 1 mg and 2.5 mg chewable tablets contain the active substance meloxicam and this was a generic application, the reference product being Metacam tablets. The active substance, meloxicam, is a well-known non-steroidal anti-inflammatory drug in veterinary medicine. Its primary mode of action is inhibition of cyclo-oxygenases in the arachidonic acid inflammatory pathway. It is beneficial in the alleviation of inflammation and pain in both acute and chronic musculoskeletal disorders.

In line with the requirements for demonstration of bioequivalence, studies on bioequivalence were furnished which showed that the 2.5 mg tablets, the highest strength, were bioequivalent in the dog. Appropriate dissolution studies allowed to also conclude on bioequivalence for the 1 mg strength tablet.

The product is presented as chewable tablets with pork flavour for easy administration to dogs.
The risks identified for these products are strictly the same as those that exist for the reference product. The excipients do not pose any additional risks.

The SPC is identical to that of the reference product for all points and thus also for risk management or mitigation. Bioequivalence has been demonstrated between Rheumocam 1 and 2.5 mg chewable tablets. Therefore, the benefits and risks expected for these products are largely identical to those of the reference product Metacam 1 and 2.5 mg tablets. The excipients do no pose any additional risks. Since bioequivalence has been demonstrated, it is expected that the conclusions about safety and efficacy are the same as those for the originator product.

The overall benefit risk evaluation is deemed positive with a sufficiently clear and complete SPC and product literature.

Based on the original and complementary data presented, it is concluded that the quality, safety and efficacy of Rheumocam chewable tablets 1 and 2.5 mg for dogs were considered to be in accordance with the requirements of Directive 2001/82/EC, as amended.