Directive 98/8/EC concerning the placing biocidal products on the market

Inclusion of active substances in Annex I or IA to Directive 98/8/EC

Assessment Report

CARBON DIOXIDE

PT 14

(Rodenticides)

29 November 2007

Annex I&IA - France

Assessment report for the active substance

Carbon dioxide (PT 14)

Finalised in the Standing Committee on Biocidal Products at its meeting on 29 November 2007 in view of its inclusion in Annex I & IA to Directive 98/8/EC

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of carbon dioxide as product-type 14 (rodenticides), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with a view to the possible inclusion of this substance into Annex I or IA to the Directive.

Carbon dioxide (CAS no. 124-38-9) was notified as an existing active substance, by Rentokil Initial plc, hereafter referred to as the applicant, in product-type 14.

Commission Regulation (EC) No 2032/2003 of 4 November 2003[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 10 of that Regulation, the Commission designated France as Rapporteur Member State to carry out the assessment of carbon dioxide on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for carbon dioxide as an active substance in product-type 14 was 28 March 2004, in accordance with Annex V of Regulation (EC) No 2032/2003.

On 25 March 2004, the French competent authority received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation, taking into account the supported uses, and confirmed the acceptance of the dossier on 31 August 2004.

On 15 May 2006, the Rapporteur Member State submitted, in accordance with the provisions of Article 10(5) and (7) of Regulation 2032/2003, to the Commission and the applicant a copy of the evaluation, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 30 May 2006. The competent authority report included a recommendation for the inclusion of carbon dioxide in Annex IA to the Directive for product-type 14.

In accordance with Article 12 of Regulation (EC) 2032/2003, the Commission made the competent authority report publicly available by electronic means on 5 October 2006. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

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1 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market, OJ L 123, 24.4.98, p.1

2 OJ L 307, 24.11.2003, p. 1

In order to review the competent authority report and the comments received on it, the European Commission organised consultations of technical experts from all Member States (peer review). Revisions agreed upon were presented at technical and competent authority meetings and the competent authority report was amended accordingly.

On the basis of the final competent authority report, the Commission proposed the inclusion of carbon dioxide in Annex IA to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on 21 June 2007.

As an active substance listed in Annex IA should normally also be listed in Annex I, the Rapporteur Member State subsequently recommended to consider the inclusion of carbon dioxide in Annex I. The inclusion in Annex I would cover those uses for which products may be expected to satisfy the requirements of Article 5 of Directive 98/8/EC, but not those of low-risk products. Such is the case of certain biocidal products used as rodenticides and containing carbon dioxide.

On the basis of this additional recommendation, the Commission also proposed the inclusion of carbon dioxide in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on 29 November 2007.

In accordance with Article 11(4) of Regulation (EC) No 2032/2003, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as last amended during its meeting held on 29 November 2007.

1.2. Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include carbon dioxide in Annex I and IA to Directive 98/8/EC for product-type 14. The aim of the assessment report is to facilitate the authorisation and registration in Member States of individual biocidal products in product-type 14 that contain carbon dioxide as an active substance. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of the assessment report, which is available at the Commission website[3], shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Directive 98/8/EC, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

1.3. Overall conclusion in the context of Directive 98/8/EC

The overall conclusion from the evaluation is that it may be expected that rodenticides containing carbon dioxide will fulfil the requirements laid down in Article 5 of Directive 98/8/EC. This conclusion is however subject to:

3 http://ec.europa.eu/comm/environment/biocides/index.htm

i. compliance with the particular requirements in the following sections of this assessment report,

ii. the implementation of the provisions of Article 5(1), and

iii. the common principles laid down in Annex VI to Directive 98/8/EC, for rodenticides containing carbon dioxide.

Furthermore, these conclusions were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at Member State level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI of Directive 98/8/EC.

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Identity, Intended Uses, Efficacy and Classification of the Active Substance

2.1.1. Identity & Analysis

Carbon dioxide has been evaluated for its use as a rodenticide (product-type 14). In its use as a rodenticide, carbon dioxide is released from a ready-for-use gas canister, at a concentration of 100 % (v/v) in a mousetrap called RADAR. The aerosol canister used in RADAR contains 2.8 g of pressurised CO_2 (actually from 2.5 to 3.0 g due to manufacturing tolerances; since 3.0 g was used as worst case for the risk assessment, both 2.8 and 3.0 values can be found in the dossier, depending on the end-point considered). The device is designed to be placed along wall-floor junctions where mice are likely to run. The unit has entrances at each end through which mice can enter. Once inside, the mouse activates a pressure pad which causes the doors to shut, trapping the mouse inside, creating therefore a sealed chamber. In the same action that closes the doors, a second mechanism causes CO_2 to be totally released from the aerosol canister. The concentration of carbon dioxide reached within the first minute of exposure is of maximum 65-67% (about 1.2 g/l) carbon dioxide, which is sufficient to kill the mouse inside the trap. Afterwards, the RADAR unit will progressively release the carbon dioxide in the room over about 15 minutes.

The active substance is defined as carbon dioxide (CAS 124-38-9), with purity > 99% (v/v).

The infra-red method for analysing the active substance, as manufactured, has been validated and shown to be sufficiently specific, accurate and precise. It can be used for analysis of carbon dioxide in air. In contrast, it has not been considered necessary to submit analytical methods in environment matrices because the exposure assessment has shown that there is no mechanism for carbon dioxide to be released directly into soil or water because it is a gas.

Furthermore, the evaluation has established that there are no additives present in carbon dioxide as notified by Rentokil Initial plc, nor any impurities above the concentration limit of 1 g/kg.

2.1.2. Intended Uses

The participant requested an inclusion of carbon dioxide in Annex I or IA for its use as rodenticide (product-type 14) against mice and rats, for professional use. However, efficacy studies presented in the dossier were only performed in mice.

2.1.3. Efficacy

In its application as a rodenticide, studies have demonstrated a sufficient degree of efficacy against mice. The biocidal action of carbon dioxide is primarily due to it causing "respiratory acidosis" in target animals. Once released, the carbon dioxide reaches the maximum concentration of 66% in the RADAR within 45 seconds; and 4 minutes later on, declines to approximately 30%. Complete release time from the RADAR into the surrounding environment exceeds 15 minutes. Carbon dioxide levels build up in the blood causing staggering, panting, coma and ultimately death, which occurs probably within the first minute (time when no more

movements were observed). These observations were performed in three mice with body weight ranging from 14.5 to 17.8 g, which corresponds to 3 or 4-week old mice. Since this age corresponds to newly weaned mice and as far as unweaned mice are not assumed to leave their nest, it is very unlikely that younger mice could be trapped and resist to carbon dioxide (because of the higher resistance of neonatal haemoglobin to carbon dioxide) and eventually die from starvation. Therefore, in accordance to the criteria usually used for judging about humaneness of pesticides, it can be considered that carbon dioxide does not cause unnecessary pain and suffering to mice.

The development of resistance to carbon dioxide is not possible because, when it is used as a biocide, it will be lethal to the target rodent in a single dose. Killing the target rodent in a single dose means that no mechanism for resistance to carbon dioxide can be developed because target organisms are never exposed to sub-lethal concentrations of carbon dioxide (as a biocide), unlike the multi-feed pesticides such as anticoagulant rodenticides.

2.1.4. Classification

In spite of the teratogenicity studies presented in the dossier, which are reporting malformations and effects on fertility, the Rapporteur Member State did not recommend to classify carbon dioxide as a substance toxic to reproduction on the basis of the following arguments:

Four studies are actually presented in the dossier by the applicant to set out the possible teratogenic effects of carbon dioxide.

1. In the first study, female Sprague-Dawley rats were exposed to 6% carbon dioxide for a single 24h-period. Increased abnormalities (intraventricular septal changes and skeleton) to the young born were observed.

2. In the second study, Wistar male rats were exposed to 2.5%, 5.0% or 10.0 % carbon dioxide for 1,2,4 or 8h. This study indicates adverse effects to male testis tissue of rats exposed to 2.5% -10% carbon dioxide. The changes were positively associated with the concentration of carbon dioxide and the duration of treatment.

3. In the third study, Swiss male mice were exposed to 65%/35% mixture air/carbon dioxide for a total of either 6h (intermittent exposure over 8h) or 26.5 h (intermittent exposure over 6 days). Adverse effects to the morphology of spermatozoa of mice and to their fertility were observed.

4. In the last study, female rabbits were exposed to 10-13% carbon dioxide for 4 to10h, on 2 or 3 different days, between gestation days 7 and 12. Skeletal abnormalities in foetuses were observed.

As emphasised by the applicant and agreed, “it is duly acknowledged that the studies have major methodological and reporting deficiencies and the data have not been generated in accordance with scientifically acceptable protocols” (reliability indices: 3). From these studies, no maternal toxicity was reported and no NOAEL could be established: indeed, studies have indicated

adverse effects from the lowest concentration tested or for the only dose tested. Moreover, it can be noticed that the tested concentrations are quite elevated.

The effects observed are no specific effects, linked to the decreased levels of oxygen in the organisms. This argument is summarised by the applicant in the study conclusions: “it is unclear from these data whether the observed effects were due to the carbon dioxide *per se* or to a secondary effect such as acidosis, increased blood flow or increased oxygen tension (secondary to hyperventilation caused by increased carbon dioxide)”. This statement was supported by the Rapporteur Member State and is in compliance with the Commission Directive 2001/59/EC related to classification, packaging and labelling of dangerous substances: “Chemicals should not be classified as toxic to reproduction where effects are solely produced as a non-specific secondary consequence of other toxic effects”.

At last, based on experimental studies, only one NOAEL has been determined from an inhalation repeated toxicity study in monkeys exposed to carbon dioxide for 93 days.

Effects of excessive carbon dioxide exposure in humans are well reported in the product literature: exposure to 1% carbon dioxide has little effect on blood parameters, exposure to 1.5% carbon dioxide led to lower heart rate, reduced tolerance to vigorous exercise, exposure to 3% carbon dioxide leads to deeper breathing, headache, reduced hearing ability, increased heart rate and acidosis. At 5-10% carbon dioxide, in addition to the effects detailed for exposure to 3% carbon dioxide, there is more a laborious breathing and a loss of judgement. At 10% carbon dioxide, in addition to the symptoms detailed for 5-10% carbon dioxide, there is also a loss of consciousness. The effects associated with carbon dioxide exposure are reversible once the carbon dioxide has been removed. Epidemiological studies do not report any toxic effects to humans after chronic exposures to carbon dioxide.

Based on the human general toxicity and the lack of human information available on teratogenicity, the limited evidence in animals studies (exposure to high levels of carbon dioxide during gestation, poor reliability indices) and the origin of the non specific effects observed in the animal studies performed with carbon dioxide, the classification of carbon dioxide as toxic to reproduction is not justified at the present state of knowledge.

There is an extensive database of information available on carbon dioxide. No critical end points in terms of adverse effects on health and environment and of physico-chemical properties have been identified for carbon dioxide. These findings are consistent with its classification for supply under 67/548/EEC, as non-hazardous for health, environment and physico-chemical effects. This classification should remain unchanged.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification

The biocidal action of carbon dioxide is primarily due to the "respiratory acidosis" induced in target animals. Carbon dioxide levels build up in the blood causing drowsiness, leading to stupor,

coma and ultimately death. Death occurs very quickly if carbon dioxide levels in the blood do not fall.

A justification for non submission of data was provided by the applicant for almost all the endpoints. This important amount of waivings was justified by the following points:

- The principal route of exposure to carbon dioxide is via inhalation. Carbon dioxide is a gas, making the potential exposure via the inhalation route more important than by the oral or dermal routes, and the latter routes are likely to be unimportant in the context of the representative biocidal product, RADAR. Accordingly, exposures via the oral and dermal routes were not considered further.

- One of the most recursive justifications for non submission of data is based on the low exposure potential of the substance during its use (cf. 2.2.1.3, Professional users).

- Carbon dioxide is naturally produced by the body, and is effectively regulated by a series of homeostatic mechanisms designed to maximise the carbon dioxide-carrying capacity of the blood. Cells produce carbon dioxide as part of the normal catabolic process.

- There is an extensive database of information available on carbon dioxide.

This database gives a coherent toxicological profile of the substance (cf. 2.2.1.2).

Although CO_2 can not be considered as an inert gas, taking into account all of these data and the negligible exposure and health risk of the product, the justifications for non submission of data were accepted.

2.2.1.2. Effects assessment

Effects can be observed in humans at acute doses and during subchronic exposure: from a slight increase of breathing and heart rates at 2-3% (v/v) CO_2, panting and tachycardia at 5-6%, to respiratory and heart distress and loss of consciousness at 10% and finally death if the exposure is not quickly stopped. These effects are linked with acidosis. Toxicity to fertility (morphological changes of spermatozoa in mice at 1% and testicular changes in rats at 2.5%) and teratogenicity (cardiac and skeletal abnormalities in rats at 6%; skeletal abnormalities in rabbits at 10%) were also observed. For that kind of effects, the mechanism of action is uncertain.

Although none of the studies were conducted following modern standards or guidelines, several studies were evaluated as acceptable as they were conducted under good scientific principles and they gave indication of the toxicological profile of carbon dioxide.

Based on the animal data provided by the applicant, no NOAEL could be determined since effects were observed from the first concentration tested excepted for the Stein *et al.* study, in which no adverse effect were observed on monkeys exposed to 3% carbon dioxide (NOAEL = 3%). In studies conducted in humans, no NOAEL could be reported either.

The maximum tolerated concentration of 10% in humans has been chosen for acute exposure as the highest non-fatal (loss of consciousness) concentration. For short-term occupational

exposure, the occupational exposure limit in the UK 1.5% (27mg/l, 15-minute time weighed average, EH40/2002) has been chosen. This choice was preferred to the derivation of a reference concentration from NOAEL and LOAEL determined in the available animal studies because of their poor reliability and above all because it was considered as being better adapted to exposure scenario. Actually**,** the choice of a 15-minute reference time is based on the discontinued exposure of the pest control technician (preferred to the long-term occupational exposure limit of 0.5%, 8-hour time weighted average recommended by the directive 2006/15/EC[4]) and is consistent with the duration of the complete release of CO_2 from the RADAR unit into the atmosphere, which is also approximately 15 minutes.

2.2.1.3. Exposure assessment

- Production operators

Using the appropriate engineering controls (n.b. manufacture occurs in a closed system under pressure), plant workers are not expected to be exposed to any carbon dioxide during its manufacture. However, as a precaution, air monitoring at the plant is assumed to ensure carbon dioxide levels never increase above the established maximum occupational exposure limit in the UK for safe working conditions (0.5% or 9150 g/m^3, 8-hour time weighted average, EH40/2002). Similarly, any carbon dioxide introduced during the manufacture of the representative product RADAR is present in a closed system. It has been concluded that the engineering controls intrinsic in both carbon dioxide and RADAR production, together with operator training and the availability of personal protective equipment (PPE) ensure health risk is minimal as the exposure of workers to carbon dioxide.

- Professional users

Although the aerosol canister used in the RADAR unit contains on average 2.8 g of pressurised CO_2, the applicant decided to base the exposure assessment on a worst-case value of 3.0 g. It has been shown that if a single RADAR unit is used in a 25 m^3 room (ex: dimensions of 2.5*4.0*2.5m), and the entire content of the aerosol is released, the volume of CO_2 will be of 1.667 litres and its concentration in the room of approximately 0.007% (v/v). The normal atmospheric concentration of CO_2 is 0.03 % (v/v). So the release of CO_2 from a RADAR unit would increase the concentration to 0.037 % (v/v), which is within normal atmospheric ranges for CO_2. Four to five RADAR units would have to release CO_2 together to double the atmospheric concentration of carbon dioxide in this kind of room. This calculation assumes that the CO_2 is immediately released into a completely airtight room. In practice, the RADAR unit will contain the CO_2 and release it over a period of over 15 minutes. The room is also likely to have some airflow, which will help to dissipate the CO_2. Thus, the levels of CO_2 in the room are unlikely to ever reach the calculated levels.

[4] Directive 2006/15/EC of 7 February 2006 establishing a second list of indicative occupational exposure limit in implementation of Council Directive 98/24/EC and amending Directives 91/322/EEC and 2000/39/EC.

The amount of CO_2 released by a RADAR unit can also be compared to the CO_2 produced by a person sitting in the room. At rest, a person will breathe about six litres of air per minute, with the exhaled air containing around 5% CO_2. In one minute, the amount of CO_2 exhaled will be (6 x 5/100) = 0.3 litre, so in six minutes the person will have exhaled 1.8 litres of CO_2, more than is released by a RADAR unit over fifteen minutes.

➢ Bystanders

As far as RADAR does not induce CO_2 concentration increase outside of the normal atmospheric range (as explained in the previous paragraph), bystanders are not more exposed to CO_2 than their usual day-to-day exposure.

2.2.1.4. Risk characterisation

➢ Production operators

Considering that CO_2 is manufactured in closed system, with air monitoring at the workplace and available PPE, trained production operators are not at risk.

➢ Professional users

Primary exposure to the professional user is considered to be unlikely and trivial. Under worst case conditions, the risk characterisation for the use of carbon dioxide in the representative biocidal product, RADAR, shows that there is no elevation of carbon dioxide levels in the atmosphere outside normal environmental ranges. Given this, and the fact that atmospheric carbon dioxide levels are well below the agreed maximum exposure limits for short-term safe working conditions with carbon dioxide (1.5% or 27 g/m^3, 15-minute time weighted average), it is considered that personal protective equipment is not necessary during the normal use of RADAR as a rodenticide. The risk from the use of carbon dioxide as a rodenticide in RADAR is considered negligible given the expected exposures (as described above). In addition, there is a significant margin of safety for both acute and repeated dose effects by inhalation. Actually, the quantities of CO_2 to be released in order to reach the limit concentrations of 1.5% and 10% in a 25-m^3 room are respectively 690 g and 4500 g. Considering that a canister only contains 3 g, the estimated margins of safety have been calculated to be 1,500 for acute exposure and 230 for repeated dose exposure**.**

➢ Bystanders

Secondary exposure to bystanders is expected to be even lower than that of professional users. In a worst-case scenario, both risks might be comparable.

2.2.2. Environmental Risk Assessment

The environmental section of the carbon dioxide dossier is reduced, mainly due to the nature of the active substance “carbon dioxide”, well-known, naturally occurring and omnipresent in the environment, and to the low environmental exposure to the substance used as rodenticide.

2.2.2.1. Effects assessment

For most of the endpoints, no standardized studies were submitted and a justification for non-submission of data was provided. This has been discussed during the 9th Technical Meeting in February 2003 where it was recommended that, for environmental properties, data on CO_2 were not required, and where relevant, data could come from literature.

The reasons invoked for waiving were mainly the followings:

- One of the most recursive justifications for non-submission of data is the low exposure potential of the substance for each compartment of the environment during its use.

- The second justification for non-submission is the low scientific relevance of some ecotoxicological tests for carbon dioxide (*e.g.* ready biodegradation (CO_2 release is the final end point measured in some of these tests), toxicity to algae, toxicity to terrestrial plants (role of CO_2 in photosynthesis…).

However, in some cases, (*e.g* acute toxicity to fish, aquatic invertebrates and earthworms), experimental data were submitted to give complementary information on the ecotoxicological response to carbon dioxide. However, they were not standardized studies and did not give suitable results for deriving a PNEC: they have therefore not been included in the overall summary or in the risk assessment.

Based on the lack of exposure of the environmental compartments and in the absence of reliable standardized studies, it was concluded that a PNEC derivation was not necessary.

2.2.2.2. Exposure assessment

The exposure assessment was discussed within the European expert group of testing strategies and accepted by the Member States. In fact, the document entitled "*Refined Waiving Concept For Rodenticides - Addendum to the Technical Notes for Guidance on Data Requirements, Chapter 1.4 (Guidance on non-submission of data)*", the section 1.4.1 "*Specific considerations for some product types*." stipulates that: "*The use of carbon dioxide as a rodenticide, under normal conditions of use, will not cause any detectable elevation in the level of carbon dioxide found naturally in air. Indeed, the volume of carbon dioxide in one trap, which gets released to atmosphere over 15 minutes, is equivalent to the amount released in an enclosed 25 m^2 room by one person breathing for six minutes*". Therefore, it has been agreed at the EU level that carbon dioxide environmental concentrations will not be affected by the use of carbon dioxide in the rodenticide product RADAR.

The exposure assessment shows that:

- There will be no exposure of the aquatic environment to carbon dioxide. Consequently, adverse effects to aquatic organisms and sediment dwelling organisms from the use of carbon dioxide in the rodenticide product, RADAR does not need to be considered.

- The use pattern proposed for the biocidal product, RADAR, means that carbon dioxide will not enter sewage treatment plants and effects on micro-organisms in sewage treatment plants does therefore not need to be considered either.

- Similarly for the terrestrial and atmospheric environmental compartments, there will be no increase in the levels of carbon dioxide in the atmosphere or soil outside normal atmospheric ranges from the use of carbon dioxide as a rodenticide.

The PEC was set to zero for all the compartments, meaning that the use of carbon dioxide as a biocide in RADAR will not increase carbon dioxide concentrations outside natural ranges.

2.2.2.3. Risk characterisation

Given the effectively zero level of exposure expected in all environmental compartments from the use of carbon dioxide as a rodenticide, it has been concluded that there is no risk to the environment or wildlife.

2.3. List of endpoints

In order to facilitate the work of Member States in granting or reviewing registrations and/or authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the most important endpoints, as identified during the evaluation process, are listed in Appendix II.

3. DECISION

3.1. Background to the Decision

The carbon dioxide dossier has been submitted by Rentokil Initial for its use as a rodenticide in the reference product "RADAR". RADAR is the mouse-trap containing a pressurised gas canister filled with approximately 2.8 g carbon dioxide at 100 % (v/v). RADAR is intended for use by Rentokil Pest Control Service staff only, as part of the Rentokil Pest Control Service, for mice.

The evaluation of the dossier led to the following conclusions concerning carbon dioxide as rodenticide:

- The substance is correctly identified with a purity > 99 % (v/v). No additive or impurity is above the concentration limit of 1 g/kg.

- There is no concern regarding the physico-chemical properties.

- The submitted information on carbon dioxide content (2.5 to 3.0 g) in RADAR is not supported by experimental data. Specifications (target-value and tolerance range) should be provided.

- The submitted information on RADAR proves that carbon dioxide is sufficiently effective against weaned mice. Efficacy claim was presented also against rats by the applicant, but not supported by experimental studies in rats. It has been estimated that carbon dioxide can be accepted as a rodenticide against mice for inclusion in Annex IA. Actually, carbon dioxide is considered as a method causing no unnecessary pain and suffering of rodent dispatch given that it leads to unconsciousness and ultimately death very quickly.

- The health effects of carbon dioxide are well documented and the toxicological profile in the light of exposure resulting from the use of this substance in RADAR is of no concern. The conclusion of the toxicological assessment is that the risk for production operators, professional users and by-standers (with estimated margins of safety calculated as 1,500 for acute exposure and 230 for repeated dose exposure) is negligible.

- The ecotoxicological assessment shows that environmental natural concentrations are not affected by the use of carbon dioxide as rodenticide and there are no critical endpoints in terms of adverse ecotoxicological effects. It was concluded that there is no risk for environment and wildlife.

- No classification and labelling is proposed for carbon dioxide, given the lack of critical endpoints in terms of adverse effects on health and environment, and of physico-chemical properties.

3.2. Decision regarding inclusion in Annexes I and IA

In view of the above, it is concluded that carbon dioxide shall be included in Annex IA of Directive 98/8/EC as an active substance for use in product-type 14 (rodenticides), subject to the following specific provisions :

- The active substance, as manufactured, shall have a minimum purity of 990 ml/l.

- Only for use in ready-for-use gas canisters functioning together with a trapping device.

Furthermore, in accordance with the principles of the Technical Note for Guidance on Annex I inclusion, carbon dioxide shall also be included in Annex I of Directive 98/8/EC as an active substance for use in product-type 14 (rodenticides), subject to the following specific provisions :

- The active substance, as manufactured, shall have a minimum purity of 990 ml/l.

It must however be noted that not all potential uses have been evaluated at the Community level. It is therefore appropriate that Member States assess those risks to the compartments and populations that have not been representatively addressed in the Community level risk assessment and, when granting product authorisations, ensure that appropriate measures are taken or specific conditions imposed in order to mitigate the identified risks to acceptable levels.

3.3. Factors to be taken into account by Member States when authorising or registering products

- Efficacy has been supported by experimental data on the reference product in mice only. A specific care shall be taken concerning the efficacy of biocidal products on other target organisms.

- The carbon dioxide content of rodenticide biocidal products should be sufficiently documented.

- The size of the ready-for-use trapping device shall be designed in function of the target organisms.

- The use of a ready-for-use trapping device by non-professional users was not evaluated in the active substance review program, as there was no claim by the notifier. Member States should be able to register or authorise a ready-for-use trapping device for non-professionals if the risks of the intended use are deemed comparable to the professional ones.

- Only the use of carbon dioxide in a ready-for-use trapping device has been evaluated at Community level, which corresponds to a low risk biocidal product. Other uses of carbon dioxide as a rodenticide (for instance, fumigation), and the associated risks, will have to be assessed at the time of the product evaluation. Such uses may lead to higher occupational exposure than the use in ready-for use trapping device. The sale and use of products may have to be restricted to professionals trained to use them, and risk mitigation measures (such as setting unprotected re-entry time) may have to be taken in order to prevent carbon dioxide concentrations in the treated space from reaching the level that was established as the short-term occupational exposure limit.

3.4. Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the inclusion of carbon dioxide on to Annex I and IA of the Directive 98/8/EC.

3.5. Updating this Assessment Report

The technical information in this assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in articles 7, 10.4 and 14 of Directive 98/8/EC. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the inclusion of carbon dioxide in Annex I or IA of the Directive.

Appendix I : List of endpoints

Identity, Physical and Chemical Properties

Identity

Chemical name (IUPAC)	Carbon dioxide
Chemical name (CA)	Carbon dioxide
CAS No	124-38-9
EC No	204-696-9
Other substance No.	None known.
Minimum purity of the active substance as manufactured	> 99% v/v carbon dioxide (990 ml/l).
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured	No additives present in carbon dioxide. No impurities present in carbon dioxide above the concentration limit of 1g/kg. No impurities of toxicological or ecotoxicological significance present below the concentration limit of 1g/kg.
Molecular formula	CO_2
Molecular mass	44.01 g/mol
Structural formula	O=C=O

Physical and chemical properties

Melting point	Sublimation temperature: -78.5ºC. Purity of carbon dioxide not available.
Boiling point	Not relevant, due to sublimation properties.
Temperature of decomposition	> 300°C under normal pressure
Appearance	Odourless, colourless gas (when >99.9% purity) under normal temperature et pressure conditions
Relative density	1.527 (where air = 1). Purity of carbon dioxide not available. The density is 1.977 g/l at 0°C
Surface tension	No surface activity is expected due to chemical structure of the substance.
Vapour pressure	Not applicable, as carbon dioxide is a gas. In

	literature the vapour pressure is 57300 hPa at 20°C.
Henry's law constant	The Henry's law constant is calculated with the following literature data: P: 57300 hPa at 20°C and solubility is 1.61 g/l at 20°C. The calculated value is: 156632 $Pa.m^3.mol^{-1}$
Solubility in water	88 ml carbon dioxide in 100 ml water at 20°C or 1.61 g/l at 20°C.
Solubility in organic solvents	Soluble in cyclohexanol (677 cm^3 CO_2/l cyclohexano or 1.2 g/l at 26°C)
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable. No organic solvents are used in the manufacture of carbon dioxide and no organic solvent is involved in the integration of carbon dioxide in the RADAR.
Partition coefficient (log P_{OW})	n-octanol/water: 0.83 Isobutanol/water: 2.26 Olive oil/water: 1.74 Temperatures not available.
Hydrolytic stability (DT_{50})	Dissolved carbon dioxide will react with water to form carbonic acid. $CO_2 + H_2O \leftrightarrow H_2CO_3$ Carbonic acid will undergo further reactions to produce bicarbonate and carbonate ions. $H_2CO_3 + OH^- \leftrightarrow HCO^-_3 + H_2O$ $HCO^-_3 + OH^- \leftrightarrow CO_3^{2-} + H_2O$ The equilibrium constant for the disassociation reaction is 600. Carbon dioxide is considered to be hydrolytically stable.
Dissociation constant	Not applicable, as carbon dioxide is a gas.
UV/VIS absorption (max.)	140 nm
Photostability (DT_{50})	Not possible to determine, as approved test guidelines are designed to work with water-soluble, non-volatile organic substances. Carbon dioxide, although water soluble, is volatile and inorganic.
Quantum yield of direct phototransformation in water at $\Sigma > 290$ nm	Not applicable
Flammability	Non flammable gas
Explosive properties	Carbon dioxide does not exhibit explosive properties.

Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	As carbon dioxide is a gas, oral exposure will not be a significant route of exposure.
Rate and extent of dermal absorption:	As carbon dioxide is a gas, dermal exposure will not be a significant route of exposure.
Distribution:	Carbon dioxide is constantly produced by the body as a result of the numerous metabolic reactions involving carbon-containing compounds. An adult man, at rest, can be expected to contribute approximately 12 litres of carbon dioxide per hour to his blood stream. If undergoing sustained work, carbon dioxide production can increase to around 100 litres of carbon dioxide per hour. The body has an ability to excrete carbon dioxide in amounts which correspond to over 12,000 mEq of acid per day without causing any toxic effects. The risk assessment for human health shows that the use of carbon dioxide in Rentokil Initial's rodenticide products does not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges. We can therefore expect it to be metabolised in the same way as the carbon dioxide naturally inhaled into the body as part of ventilation, and that produced by respiring cells.
Potential for accumulation:	Refer to "Distribution" (above).
Rate and extent of excretion:	Refer to "Distribution" (above).
Toxicologically significant metabolite	Refer to "Distribution" (above).

Acute toxicity

Rat LD_{50} oral Rat LD_{50} dermal	Not applicable, as carbon dioxide is a gas. Principle route of exposure will be by inhalation.
Inhalation	10% carbon dioxide (man): not fatal to man (although the effects experienced were very unpleasant). This value has been used for the risk assessment for acute exposures to carbon dioxide.
Skin irritation	Not technically possible to determine the skin irritation potential of carbon dioxide using conventional techniques because it is a gas. However, it should be noted that the risk assessment for human health shows that the use of carbon dioxide in Rentokil Initial's rodenticide products does not cause any elevation of carbon

	dioxide in air, outside normal atmospheric ranges.
Eye irritation	Not technically possible to determine the eye irritation potential of carbon dioxide using conventional techniques because it is a gas. However, it should be noted that the risk assessment for human health shows that the use of carbon dioxide in Rentokil Initial's rodenticide products does not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges.
Skin sensitization	Not technically possible to determine the skin sensitisation potential of carbon dioxide using conventional techniques because it is a gas. However, it should be noted that the risk assessment for human health shows that the use of carbon dioxide in Rentokil Initial's rodenticide products does not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges.

Repeated dose toxicity

Species/ target/critical effect	The long-term occupational exposure limit for carbon dioxide set in the UK is 5,000 ppm / 0.5% (8 hour time weighted average) while the short term occupational exposure limit is 15,000 ppm / 1.5% (15 minutes reference period)[5].
Lowest relevant oral NOAEL/LOAEL Lowest relevant dermal NOAEL/LOAEL	Not applicable, as carbon dioxide is a gas. Principle route of exposure will be by inhalation.
Lowest relevant inhalation NOAEL/LOAEL	The long-term occupational exposure limit for carbon dioxide set in the UK is 5,000 ppm / 0.5% (8 hour time weighted average) while the short term occupational exposure limit is 15,000 ppm / 1.5% (15 minutes reference period)[6]

5 Existing data on the subchronic toxicity of carbon dioxide are available, including data on man. However, it is acknowledged that this data, was carried out some time ago, and was therefore not carried out to current protocols or with current laboratory techniques. Given that this data is unavoidably weak, the current occupational exposure limit for safe working conditions with carbon dioxide has been used as the NOAEL value for the risk assessment. This is because the use of carbon dioxide as a rodenticide does not increase carbon dioxide above levels found naturally in the atmosphere, and this is well below established maximum occupational exposure limits for safe working conditions.

6 Occupational exposure work has been carried out in humans exposed to an environment with high $paCO_2$ values such as brewery workers. Such data have been used previously by a number of regulatory authorities to set national, international and supranational maximum exposure limits for safe working conditions, and all of these exposure limits are in general agreement.

Genotoxicity	It is not technically possible to determine the genotoxic potential of carbon dioxide using conventional *in vitro* techniques because carbon dioxide is present naturally in the environment and it is also naturally produced by all aerobic cells as a by-product of respiration. This makes it impossible to remove it from negative controls. However, it should be noted that the risk assessment for human health shows that the use of carbon dioxide in Rentokil Initial's rodenticide products does not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges.

Long term toxicity

Species/target/critical effect	
Lowest relevant NOAEL/LOAEL	

Carcinogenicity

Species/type of tumour	It is not considered scientifically necessary to determine the carcinogenic potential of carbon dioxide for a number of reasons including: 1. The risk assessment for human health shows that the use of carbon dioxide in Rentokil Initial's rodenticide products does not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges. 2. The potential for exposure to carbon dioxide when it is manufactured and used as a rodenticide is minimal because it is manufactured in a completely enclosed system. The use pattern for RADAR has determined that, under worse case conditions, one person could be exposed to 3.0g carbon dioxide (note that this is extremely unlikely). If this level of exposure occurred the person would still be exposed to levels a lot lower than the maximum occupational exposure limits set for safe working conditions with carbon dioxide. 3. The maximum exposure limits for safe working conditions are well established for carbon dioxide, and all of these exposure limits are in general agreement. The use of carbon dioxide

	in Rentokil Initial's rodenticide products do not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges, and this is well below these agreed maximum exposure limits for safe working conditions. As the objective of an animal test is to predict the toxicological effect in humans, then an established safe exposure limit based on human takes precedence over animal data generated for the approximation of a theoretical safe value. 4. While it is possible to carry out a carcinogenic study on carbon dioxide, it will be technically very difficult, full of constraints and very expensive. The body's metabolism and physiology are extremely sensitive to carbon dioxide levels and will adjust to any atmospheric changes. This affects the body's metabolism making it difficult to differentiate any observations on the test animal as a toxic effect of carbon dioxide itself, or as a secondary effect of the body's change in metabolism. Because of this, even if the carcinogenicity study was carried out it is going to provide little useful information for the risk assessment.
Lowest dose with tumours	Refer to "Species/type of tumour" above.

Reproductive toxicity

Species/reproduction target/critical effect	Note that the risk assessment for human health shows that the use of carbon dioxide in Rentokil Initial's rodenticide products does not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges. However, there are four studies available on the possible teratogenic effects of carbon dioxide. These are: 1) Female Sprague-Dawley rats were exposed to 6% carbon dioxide for single 24h-period between gestation days 5 and 21. There were increased abnormalities (intraventricular septal changes) to the young born. Note there was also an increase in skeletal abnormalities. There was a slight increase in perinatal mortality in the test group, and a lower frequency of male offspring. The average pup weight was 18.9% higher in the test litters. 2) Wistar male rats were exposed to 2.5%, 5.0% or 10.0 % carbon dioxide for 1,2,4 or 8h. Study

	indicates adverse effects to male testis tissue of rats exposed to 2.5% - 10% carbon dioxide. The changes were positively associated with the concentration of carbon dioxide and the duration of treatment. 3) Swiss male mice were exposed to 65%/35% mixture air/carbon dioxide for a total of either 6h (intermittent exposure over 8h) or 26.5 h (intermittent exposure over 6 d). Study indicates adverse effects to the morphology of spermatozoa of mice, and their fertility when they were exposed to 35% carbon dioxide. 4) Female rabbits were exposed to 10-13% carbon dioxide for 4 to10h, on 2 or 3 different days, between gestation days 7 and 12. Skeletal abnormalities in foetuses were observed. Whilst the effects reported in all four studies above could have been attributable to carbon dioxide they might also be a response to low pH or to increased oxygen tension (secondary to hyperventilation caused by increased carbon dioxide).
Lowest relevant NOAEL	NO(A)EL has not been established. However, studies indicate adverse effects to young born under conditions of 6% carbon dioxide, adverse effects to male testis tissue of rats exposed to 2.5% -10% carbon dioxide and adverse effects to the morphology of spermatozoa of mice, and their fertility when they were exposed to 35% carbon dioxide. Note that whilst the effects reported in these studies could have been attributable to carbon dioxide they might also be a response to low pH or to increased oxygen tension (secondary to hyperventilation cause by increased carbon dioxide).
Species/developmental target / critical effect Lowest relevant NOAEL	See above.

Neurotoxicity / Delayed neurotoxicity

2-day acute neurotoxicity study in rats 13-weeks neurotoxicity study in rats 12-month chronic neurotoxicity study in rats	There is a substantial volume of data available on the toxicity of carbon dioxide, and none of it indicates that it may have neurotoxic effects. On this basis, it is not necessary to submit additional toxicity about the neurotoxicity of carbon dioxide.

Medical data

Effects of excessive carbon dioxide exposure in man are well reported in the product literature. The key results for man include the following:

Exposure to 1% carbon dioxide (time weighted average) during the working day has little effect on blood parameters, including bicarbonate and carbon dioxide. (It should be noted that the author of the study had great difficulty in monitoring the exposure of subjects to carbon dioxide because of their movements).

Exposure to 1.5% carbon dioxide led to lower heart rate, reduced tolerance to vigorous exercise. There was no apparent changes in performance or basic physiological parameters when humans were exposed to 1.5% carbon dioxide for 42 days . There was slight acidosis for 23 days, increased respiratory rate and increased systolic BP.

Exposure to 3% carbon dioxide leads to deeper breathing, headache, reduced hearing ability, increased heart rate and acidosis.

At 5-10% carbon dioxide, in addition to the effects detailed for exposure to 3% carbon dioxide there is more laborious breathing and loss of judgement.

At 10% carbon dioxide , in addition to the symptoms detailed for 5-10% carbon dioxide, there is also loss of consciousness.

It has been widely reported that the effects associated with carbon dioxide exposure are reversible once the carbon dioxide has been removed.

It should be noted that under normal conditions of use, the use of carbon dioxide in Rentokil Initial's rodenticide (PT14) products will not cause any elevation in the level of carbon dioxide in air, outside normal atmospheric ranges, and the studies available on man tend to address much longer periods of exposure than are likely to be relevant for the use of carbon dioxide in the representative product, RADAR.

Summary	Value	Study	Safety factor
ADI (if residues in food or feed)	Not applicable, as not intended for use on food or feed.		

AOEC (Operator/Worker) AOEC (Bystander)	The long-term occupational exposure limit for carbon dioxide set in the UK is 5,000 ppm / 0.5% (8 hour time weighted average) while the short term occupational exposure limit is 15,000 ppm / 1.5% (15 minutes reference period).
Drinking water limit	Not applicable, as not intended to be applied in water.
ARfD (acute reference dose)	Not applicable, as not intended to be applied on food or in water.

Acceptable exposure scenarios (including method of calculation)

Professional users	For professional users, the daily total exposures to carbon dioxide from the use of the product RADAR is expected to be 3g[7]. The release of 3g of carbon dioxide into a 25 m^3 does not increase levels of carbon dioxide outside the natural atmospheric range (0.03%)8. Given this, and the fact that atmospheric carbon dioxide levels are well below the agreed maximum exposure limits for safe working conditions with carbon dioxide (1.5% / 15,000 ppm or 27 g/m^3 15-minute time weighted average) it is considered that personal protective equipment is not necessary during the normal use of RADAR as a rodenticide. The risk from the use of carbon dioxide as a rodenticide in RADAR is considered negligible given the expected exposures (as described above).
Workers (re-entry)	
Non-professional users	Not applicable. Rentokil's RADAR unit is intended to be used by professional users only.
Indirect exposure as a result of use	As carbon dioxide is a gas, the principle route of exposure to bystanders is via inhalation. Because carbon dioxide is a gas, there is no pesticide residue present on surfaces on which people come into contact. The release of 3g of carbon dioxide into a

7 RADAR is intended for use by Rentokil Pest Control Service staff only, as part of the Rentokil Pest Control Service. The figure of 3g carbon dioxide per day has been calculated from the known sales figures of the RADAR unit in Europe and the number of Service staff using the product.

8 A calculation was made to determine the effect of 3g of carbon dioxide being released into a 25 m^3 room. This calculation shows that it does not increase levels of carbon dioxide in the room outside normal atmospheric concentrations and is equivalent to one person breathing in the room for six minutes.

25 m^3 does not increase levels of carbon dioxide outside the natural atmospheric range (0.03%) [9]. Therefore the risk to bystanders from secondary exposure to carbon dioxide attributable to the use of RADAR are no more than their normal day-to-day exposures to carbon dioxide. This level of exposure means that there is a 1,500 fold safety factor present before adverse effects can be expected to occur from acute exposure to carbon dioxide[10]. This margin of safety is considered acceptable, and therefore it is concluded that there is no risk to bystanders from the use of carbon dioxide as a rodenticide.

9 A calculation was made to determine the effect of 3g of carbon dioxide being released into a 25 m^3 room. This calculation shows that it does not increase levels of carbon dioxide in the room outside normal atmospheric concentrations and is equivalent to one person breathing in the room for six minutes.

10 To establish this 1,500 fold margin of safety, it was determined how much carbon dioxide must be released into 25 m3 room before a 10% v/v level is reached (the figure used for the risk assessment for acute exposures to carbon dioxide in man – this level was not fatal in man, but the effects experienced were very unpleasant). This volume of carbon dioxide is compared to how much exposure is expected from the normal use of RADAR in order to determine the margin of safety.

Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50})	Dissolved carbon dioxide will react with water to form carbonic acid. $CO_2 + H_2O \leftrightarrow H_2CO_3$ Carbonic acid will undergo further reactions to produce bicarbonate and carbonate ions. $H_2CO_3 + OH^- \leftrightarrow HCO^-_3 + H_2O$ $HCO^-_3 + OH^- \leftrightarrow CO_3^{2-} + H_2O$ The equilibrium constant for the disassociation reaction is 600. Carbon dioxide is considered to be hydrolytically stable.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	No data. This test is not technically feasible to perform.
Readily biodegradable	No data. Testing for the ready biodegradability of carbon dioxide is scientifically unjustified.
Biodegradation in seawater	No data. Not required (no exposure of seawater).
Non-extractable residues	No data. Not required (no exposure).
Distribution in water / sediment systems (active substance)	No data. Not required (no exposure).
Distribution in water / sediment systems (metabolites)	No data. Not required (no exposure).

Route and rate of degradation in soil

Mineralization (aerobic)	No data. Not required (not scientifically justified; no exposure).
Laboratory studies	No data. Not required (not scientifically justified; no exposure).
Field studies	No data. Not required (not scientifically justified; no exposure).
Anaerobic degradation	No data. Not required (not scientifically justified; no exposure).

Soil photolysis	No data. Not required (not scientifically justified; no exposure).
Non-extractable residues	No data. Not required (not scientifically justified; no exposure).
Relevant metabolites - name and/or code, % of applied a.i.	No data. Not required (not scientifically justified; no exposure).
Soil accumulation and plateau concentration	No data. Not required (not scientifically justified; no exposure).

Adsorption/desorption

Ka, Kd Ka_{oc}, Kd_{oc} pH dependence	In water: $CO_2 + H_2O \surd H_2CO_3$ No soil specific data. Not required (no exposure).

Fate and behaviour in air

Direct photolysis in air	No data. Not required (no exposure; not technically feasible).
Quantum yield of direct photolysis	Not applicable.
Photo-oxidative degradation in air	Not applicable.
Volatilization	Not applicable.

Monitoring data, if available

Soil	No data available. Not required (no exposure)
Surface water	No data available. Not required (no exposure)
Ground water	No data available. Not required (no exposure)
Air	No data available. Not required (no exposure)

Effects on Non-target Species

Toxicity data for aquatic species

Species	Time-scale	Endpoint	Toxicity (mg/l)

Foreword: There are no standard short term or long term toxicity tests available on carbon dioxide to fish, algae, or micro-organisms or any other aquatic organisms. It was not considered scientifically necessary to conduct these tests, because under normal conditions of use there will be no exposure of carbon dioxide in the RADAR unit to the aquatic environment.			
Fish			
Fish (*Brachydanio rerio*)			No validated data from guidelines studies. Not required (no exposure)
Invertebrates			
Invertebrate (*Daphnia magna*)			No validated data from guidelines studies. Not required (no exposure)
Algae			
Algae (*Selenastrum capricornutum*)			No validated data Not required (no exposure)
Microorganisms			
Not determined.			No validated data Not required (no exposure)

Effects on earthworms or other soil non-target organisms

Acute toxicity	No validated data from guidelines studies. Not required (no exposure)
Reproductive toxicity	No validated data from guidelines studies. Not required (no exposure)

Effects on soil micro-organisms

Nitrogen mineralization	No validated data. Not required (no exposure)
Carbon mineralization	No validated data. Not required (no exposure)

Effects on terrestrial vertebrates

Acute toxicity to mammals	No validated data. Not required (no exposure)
Acute toxicity to birds	No validated data. Not required (no exposure)
Dietary toxicity to birds	No validated data. Not required (no exposure)
Reproductive toxicity to birds	No validated data. Not required (no exposure)

Effects on honeybees

Acute oral toxicity	No validated data. Not required (no exposure)
Acute contact toxicity	No validated data. Not required (no exposure)

Effects on other beneficial arthropods

Acute oral toxicity	No validated data. Not required (no exposure)
Acute contact toxicity	No validated data. Not required (no exposure)
Acute toxicity to …….. ……	No validated data. Not required (no exposure)

Bioconcentration

Bioconcentration factor (BCF)	No validated data. Not required (not scientifically justified, no exposure)
Depuration time (DT_{50}) (DT_{90})	Refer to “Bioconcentration factor (BCF)” (above).
Level of metabolites (%) in organisms accounting for > 10 % of residues	Refer to “Bioconcentration factor (BCF)” (above).

Appendix II: List of Uses Supported by Available Data

CARBON DIOXIDE

Product type:

Rodenticide (PT14)

Claim of the participant:

For the control of rats and mice.

Target organisms:

House mouse (*Mus domesticus),*

Brown rat *(Rattus norvegicus),*

Black rat *(Rattus rattus).*

Among these claimed species, only efficacy against mice was actually tested

Concentration:

100%

Categories of users supported by the data submitted in the dossier:

Professionals

Type of application:

Single application.

Carbon dioxide is designed to be released from a gas canister into a mousetrap, placed along wall floor junctions where mice are likely to run. When the mouse is caught and killed, the mousetrap is removed and replaced by a new one.

RADAR units hereafter described are mousetraps especially developed for killing mice quickly and humanely: the unit has entrances at each end through which mice can enter. Once inside, the mouse activates a pressure pad which causes the doors to shut, trapping the mouse inside, creating a sealed chamber. In the same action that closes the doors, a second mechanism causes CO_2 to be totally released from an aerosol canister, which humanely kills the mouse inside the trap. The UK Home Office currently recommends the use of carbon dioxide in a rising concentration as a humane method of killing rodents up to 1.5 kg. Mice are initially knocked out by the narcotic effects of carbon dioxide when the concentration reaches 30% and eventually killed when the concentration reaches 70%.

The dimensions of the RADAR unit are clearly defined to ensure that the unit's length is adequate to guarantee that once the unit is triggered, the mouse –including tail -is completely inside the unit so that the animal can be dispatched quickly and humanely. The volume of carbon dioxide required to reach the 70% threshold limit specified by the UK Home Office was calculated. Different weights of animals were tested in the unit to ensure that all animals are killed quickly and humanely. Test data shows that when aerosols containing 2.35g, 2.36g and 2.38g carbon dioxide were used in the RADAR unit, carbon dioxide concentrations reached 65-67% when the unit was tripped. This concentration was sufficient to kill mice weighing 14.5g – 17.8g within one minute of the RADAR unit being tripped.

However, it is not acceptable to allow any possibility for failure to kill trapped mice (trapping a mouse without killing it would be clearly unacceptable). Therefore, in order to ensure an adequate safety margin for manufacturing tolerances and different weights of mice, aerosols are supplied for use in the RADAR unit containing 2.8g carbon dioxide. Any environmental or non-target risks posed by the extra carbon dioxide are far outweighed by the increase in reliable efficacy.

Appendix III: List of studies

CARBON DIOXIDE

Data protection is claimed by the applicant in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked “Y” in the “Data Protection Claimed Y/N” column of the four lists below (numbered 1-4). For studies marked Y(i) data protection is claimed under Article 12.1(c) (i), for studies marked Y(ii) data protection is claimed under Article 12.1(c) (ii). These claims are based on information from the applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It is not possible for the Rapporteur Member State to confirm the accuracy of this information.

Identity

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Anonymous	On-line calculation of Partition Coefficient for Carbon Dioxide http://esc.syrres.com/interkow/kowdemo.htm /			Y		N	P	Applicant's reference number: CO2 114	2002
Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295, ISBN 0911910-12-3	Merck Research Laboratories		Y		N	P		1996

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Data Owner:	A = Applicant
	P= Public domain

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
European Chemicals Bureau	Details for carbon dioxide ECB-EINECS Information System. http://ecb.jrc.it/new-chemicals/			Y		N	P	Applicant's reference number: CO2 239	2003
Federation of American Societies for Experimental Biology	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service			Y		N	P	Applicant's reference number: CO2 96	1979

Physical and Chemical Properties

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Anonymous	Ideal Gas Law - from Eric Weisstein's World of Physics. http://scienceworld.wolfram.com/physics/IdealGasLaw.html Deviations from Ideal Gas Law Behavior. http://chemed.chem.purdue.edu/genchem/topicreview/bp/ch4/deviation5.html			Y		N	P	Applicant's reference number: CO2 229	2003
Anonymous	Raoult's Law and Phase Equilibria. www.jcsu.jesus.cam.ac.uk/~rpc25/notes/chemistry/phase_equilibria/			Y		N	P	Applicant's reference number: CO2 228	2003
Anonymous	On-line calculation of Partition Coefficient for Carbon Dioxide http://esc.syrres.com/interkow/kowdemo.htm /			Y		N	P	Applicant's reference number: CO2 114	2002

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Anonymous	Octanol-Water Partition Coefficient Estimation by JAVA Applet http://www.pirika.com/chem/TCPEE/LOGKOW/ourlogkow.htm /			Y		N	P	Applicant's reference number: CO2 257	2004
Battino R, Evans FD, Danforth WF, Wilhelm E	The Solubilities of Gases in Liquids 2. The Solubility of He, Ne, Ar, Kr, N2, O2, CO, and CO2 in 2-methyl-1-propanol (1-55 oC) J Chem. Thermodynamics Vol 3 pages 743-751		N	Y		N	P	Applicant's reference number: CO2 220	1971
Battino R Evans FD Danforth WF	The Solubilities of Seven Gases in Olive Oil With Reference to Theories of Transport Through the Cell Membrane The Journal of the American Oil Chemists Society Vol 45 pages 830-833		N	Y		N	P	Applicant's reference number: CO2 230	1968
Battino R Evans FD, Danforth WF, Wilhelm E	Solubilitie de Quelques Gaz Dans le Cyclohexanol J Chem Phys Vol 24 pages 53-55.		N	Y		N	P	Applicant's reference number: CO2 223	1971

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Blanchard F, Carre B, Biensan P, Lemordant D	Study of the Carbon Dioxide Solubility in Solvent and Electrolytes used in Lithium Ion Batteries. www.univ-tours.fr/ed/edsst/comm2002/blanchard.pdf		N	Y		N	P	Applicant's reference number: CO2 255	2002
British Standard	Transportable Gas Containers - Part 7: Specification for Seamless Steel Gas Containers of Water Capacity 0.5L up to 15 L for Special Portable Applications British Standard BS 5045-7:2000. Committee Reference PVE/3 ISBN 0580 331644 / 1			Y		N	P	Applicant's reference number: CO2 181	2000
Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295, ISBN 0911910-12-3 /	Merck Research Laboratories		Y		N	P		1996
Cauquil G	Solubilitie de Quelques Gaz Dans le Cyclohexanol J Chem Phys Vol 24 pages 53-55		N	Y		N	P	Applicant's reference number: CO2 222	1927

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Chemical Sciences	Henry's Law and the Solubility of Gases From: www.psigate.ac.uk/newsite/reference/plambeck/chem2/p01182.htm /			Y		N	P	Applicant's reference number: CO2 256	2004
Ettinger R Blume P Patterson A	C13 Chemical Shifts in CO and CO2 The Journal of Chemical Physics Vol 33 No. 5 Pages 1597-1598		N	Y		N	P	Applicant's reference number CO2 213	1960
European Commission	Method A.1 Melting/freezing Temperature Classification, Packaging and Labelling of Dangerous Substances in the European Union. Part II - Testing Methods Page 9-18 Office for Official Publications of the European Communities ISBN 92-828-0076-8			Y		N	P		1997
European Commission	Method A.2 Boiling Temperature Classification, Packaging and Labelling of Dangerous Substances in the European Union. Part II - Testing Methods Page 19-25 Office for Official Publications of the European Communities ISBN 92-828-0076-8			Y		N	P		1997

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
European Commission	Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances, Commission Regulation (EC) No. 1488/94 on Risk Assessment for Existing Substances, Directive 98/8/EC of the European Parliament and of the Council Concerning the Placing of Biocidal Products on the Market, Part II. Pages 122-124			Y		N	P		2003
European Commission	Method A.9 Flash Point Classification, Packaging and Labelling of Dangerous Substances in the European Union. Part II - Testing Methods Page 78-79 Office for Official Publications of the European Communities ISBN 92-828-0076-8			Y		N	P		1997
European Commission	Method A.5 Surface Tension Classification, Packaging and Labelling of Dangerous Substances in the European Union. Part II - Testing Methods Page 51-57 Office for Official Publications of the European Communities ISBN 92-828-0076-8			Y		N	P		1997

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
European Commission	Method A.14 Explosive Properties Classification, Packaging and Labelling of Dangerous Substances in the European Union. Part II - Testing Methods Page 91-101 Office for Official Publications of the European Communities ISBN 92-828-0076-8			Y		N	P		1997
European Commission	Method A.17 Oxidisng Properties (solids) Classification, Packaging and Labelling of Dangerous Substances in the European Union. Part II - Testing Methods Page 106-110 Office for Official Publications of the European Communities ISBN 92-828-0076-8			Y		N	P		1997
Greenwood NN Earnshaw A	Chapter 8.6 Oxides and Carbonates. Chemistry of the Elements First Edition. Page 325-333 Pergamon Press plc. ISBN 0-08-022057-6			Y		N	P	Applicant's reference number: CO2 190	1984

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Lide DR Frederikse HPR	Solubility of carbon dioxide in water CRC Handbook of Chemistry and Physics - A Ready-Reference Book of Chemical and Physical Data. 76th Edition Pages 6-3 & 6-4 CRC Press Inc. ISBN 0-8493-0476-8			Y		N	P	Applicant's reference number: CO2 182	1995
Lietzke MH Mullins C	The Thermal Decomposition of Carbon Dioxide. J. Inorg. Nucl. Chem. Vol 43. pages 1769-1771		N	Y		N	P	Applicant's reference number: CO2 207	1981
Meehan AP	Rats and Mice Their Biology and Control pages 87-140 Rentokil Limited, Felcourt, East Grinstead, W Sussex RH19 2JY ISBN 0 906564 05 0			Y		N	P		1984
Stein SE	IR and Mass Spectra NIST Chemistry Webbook, NIST Standard Reference Database Number 69 Eds. P. J. Linstrom and W.G Mallard, July 2001 National Institute and Technology Gaithersburg MD 20899 http://webbook.nist.gov			Y		N	P	Applicant's reference number: CO2 178	2001

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Stein SE	IR and Mass Spectra NIST Chemistry WebBook, NIST Standard Reference Database Number 69, Eds. P.J. Linstrom and W.G. Mallard, July 2001, National Institute of Standards and Technology, Gaithersburg MD, 20899 http://webbook.nist.gov			Y		N	P	Applicant's reference number: CO2 179	2001
Stothers JB	Carbon-13 NMR Spectroscopy. Academic Press Pages 279-310		N	Y		N	P	Applicant's reference number: CO2 218	1972
Thompson BA Harteck P Reeves RR Jnr.	Ultraviolet Absorption Coefficients of CO2, CO, O2, H20, N20, NH3, NO, SO2 and CH4 between 1850 and 4000 A. Journal of Geophysical Research Vol 68, No. 24 Pages 6431-6436		N	Y		N	P	Applicant's reference number: CO2 175	1963
United States Environmental Protection Agency	EPA Product Properties Test Guidelines OPPTS 830.7370 Dissociation Constants in Water EPA 712-C-96-036			Y		N	P		1996

Analytical Methods

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Messer UK Ltd	Validation of Analytical Methods Used to Determine the Percentage Concentration of Carbon Dioxide		Y	N		Y	A	Applicant's reference number: CO2 252	2004

Effectiveness Against Target Organisms and Intended Uses

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Anonymous	Acid-Base Balance The Merck Manual of Medical Information- Home Edition . Section 12 Disorders of Nutrition and Metabolism Chapter 138. www.merck.com/mrkshared/mmanual_home/sec12/138.jsp /			Y		N	P	Applicant's reference number: CO2 237	2003
Anonymous	8-13 Resistance to Pesticides Department of the Navy Bureau of Medicine and Surgery Manual of Naval Preventive Medicine: Chapter 8: Navy Entomology and Pest Control Technology: Section II Pesticides and Their Application http://www.vnh.org/PreventiveMedicine/Chapter8/8.13.html /			Y		N	P	Applicant's reference number: CO2 238	2003
Meehan AP	Rats and Mice Their Biology and Control pages 87-140 ISBN 0 906564 05 0 /	Rentokil Limited, Felcourt, East Grinstead, W Sussex RH19 2JY		Y		N	P		1984

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Rentokil Initial plc	RADARmonitor Pen Trial		Y	N	Y	Y	A	PC165 Applicant's reference No. CO2 231	2003
Rentokil Initial plc	RADARmonitor Pen Trial		Y	N	Y	Y	A	PC166 Applicant's reference No. CO2 232	2003
Rentokil Initial plc	RADARmonitor Pen Trial		Y	N	Y	Y	A	PC167 Applicant's reference No. CO2 233	2003
Rentokil Initial plc	RADARmonitor Pen Trial		Y	N	Y	Y	A	PC168 Applicant's reference No. CO2 234	2003

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Rentokil Initial plc	RADARmonitor Pen Trial		Y	N	Y	Y	A	PC169 Applicant's reference No. CO2 235	2003
Rentokil Initial plc	RADARmonitor Pen Trial		Y	N	Y	Y	A	PC170 Applicant's reference No. CO2 236	2003
Rentokil Initial plc	Reliability and Efficacy Tests of RADAR Prototype (New 'Aerosol Version') for UK Registration Purposes. Pest Control Technical Committee Report RPC 01/07 Project 290/03		N	N	Y	Y	A	Applicant's reference number: CO2 92	2001
UK Home Office	The Humane Killing of Animals under Schedule 1 to the Animals (Scientific Procedures) Act 1986 Code of Practice The Stationery Office Limited			Y	Y	N	P	Applicant's reference number: CO2 139	1986

Toxicological and Metabolic Studies

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Alexander W, Duff P, Haldane JBS, Ives G, Renton D	After Effects of Exposure of Men to Carbon Dioxide Lancet Vol 2, pages 419-420		N	Y		N	P	Applicant's reference number CO2 195	1939
Anonymous	Environmental Management Indicators and Environmental Accounting Basic Thinking for Environmenal Management Indicators and Environmental Accounting http://www.kirinco.jp/english/company/env/p12_13.html /			Y		N	P	Applicant's reference number CO2 137	2002
Barbour JH, Seevers MH	A Comparison of the Acute and Chronic Toxicity of Carbon Dioxide with Especial Reference to its Narcotic Action. Journal of Pharmacology and Experimental Therapeutics. Vol 78 pages 11-21		N	Y		N	P	Applicant's reference number CO2 81	1942

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Blackburn JP, Conway CM, Leigh LM, Lindop MJ, Reitan JA	PaCo2 and the Pre-ejection Period: The PaCo2/Inotrophy Response Curve Anesthesiology Vol 37, No 3 pages 268-276		N	Y		N	P	Applicant's reference number CO2 133	1972
Brackett NC, Wingo CF, Muren O, Solano JT	Acid Base Response to Chronic Hypercapnia in Man The New England Journal of Medicine Pages 124-130		N	Y		N	P	Applicant's reference number CO2 200	1969
Brown EB Jr., Miller F	Ventricular Fibrillation Following a Rapid Fall in Alveolar Carbon Dioxide Concentration Am. J. Physiol Vol 169 pages 56-60		N	Y		N	P	Applicant's reference number CO2 118	1952
Consolazio WV, Fisher MB, Pace N, Pecora LJ, Pitts GC, Behnke AR	Effects on Man of High Concentrations of Carbon Dioxide in Relation to Various Oxygen Pressures During Exposures as Long as 72 Hours Am J Physiol Vol 151 Pages 479-503		N	Y		N	P	Applicant's reference number CO2 198	1947

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Cullen DJ, Eger EI	Cardiovascular Effects of Carbon Dioxide in Man Anesthesiology Vol 41, pages 345-349		N	Y		N	P	Applicant's reference number CO2 132	1974
Environmental Protection Agency	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs			Y		N	P	Applicant's reference number CO2 91	1991
Environmental Protection Agency	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs			Y		N	P	Applicant's reference number CO2 91	1991
Faucett RE, Newman PP	Operation Hideout Preliminary Report: Report No. 228 US Naval Research Laboratory New London Conn		N	Y		N	P	Applicant's reference number: CO2 140	1953

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Federation of American Societies for Experimental Biology	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service			Y		N	P	Applicant's reference number CO2 96	1979
Goodman LS, Gilman A	Goodman and Gilmans The Pharmacological Basis of Therapeutics. Sixth Edition Pages 331-334 ISBN 0-02-344720-6			Y		N	P	Applicant's reference number CO2 82	1980
Grote W	Interference with Embryo Development with Increased CO2 and O2 Partial Pressure and with Under-Pressure Z Morpholol Anthropol vol 56, pp 165-194		N	Y	Y	N	P	Applicant’s reference number CO2 278	1965
Haring OM	Cardiac Malformations in Rats Induced by Exposure of the Mother to Carbon Dioxide During Pregnancy Circulation Research, Vol VIII, pages 1218-1227		N	Y	Y	N	P	Applicant's reference number CO2 107	1960
Health and Safety Executive	EH40/2002 Occupational Exposure Limits 2002 HSE Books ISBN 0717620832			Y		N	P		2002

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
King CTG, Williams EE, Mego JL, Schaefer KE	Adrenal Function During Prolonged Exposure to Low Concentration of Carbon Dioxide Am J Physiol Vol 180, Pages 227-278		N	Y		N	P	Applicant's reference number CO2 210	1955
Kinney JM	Transport of Carbon Dioxide in Blood Anethesiology Vol 21, Number 6 pages 615-619		N	Y		N	P	Applicant's reference number CO2 150	1960
Krehl L, Straub W	Moderne Gewerbliche Vergiftungen. Naunyn-Schmiedebergs "Archiv fur Experimentelle Pathologie und Pharmakologie" pages 65-83 Verlag Von F.C.W in Leipzig		N	Y		N	P	Applicant's reference number CO2 83	1928
Luft US, Finklestein S, Elliot JC	Respiratory Gas Exchange, Acid-Base Balance and Electrolytes during and After Maximal Work Breathing 15 mmHg PICO2 Topics in Environmental Physiology and Medicine Carbon Dioxide and Metabolic Regulations Edited by Gabriel Nahas and Karl E Schaefer Pages 282 - 293 Springer Verlag New York		N	Y		N	P	Applicant's reference number CO2 155	1974

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Maiti H, Cheyne MF, Hobbs G, Jeraj HA	Cryotherapy Gas - to Use Nitrogen Oxide or Carbon Dioxide? Int J Std AIDS 1999, Feb 10 (2) 118-120		N	Y		N	P	Applicant's reference number CO2 274	1999
McDowall RJS	Chapter 15 and 16 The Respiratory System, Chapter 17 The Relation of Respiration to Other Processes in the Body Handbook of Physiology 43rd Edition Pages 171-221 John Murray, London			Y		N	P	Applicant's reference number CO2 240	1964
Messer UK Ltd	Safety Data Sheet for Carbon Dioxide (Refrigerated Liquid) dated 10/02/2000 Version 03					N	P		2000
Morita M, Tabata N	Studies on Asphyxia : on the Changes of the Alveolar Walls of Rats in the Hypoxic State. II The Hypoxic State Produced by Carbon Dioxide and Methane Gases. Forensic Science International. Vol. 39 pages 257-262			Y	Y	N	P	Applicant's reference number CO2 97	1988

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Mukherjee DP, Singh SP	Effect of Increased Carbon Dioxide in Inspired Air on the Morphology of Spermatozoa and Fertility of Mice J Reprod. Fertility Vol 13 pages 165-167		N	Y	Y	N	P	Applicant's reference number CO2 110	1967
Nahas G	Mechanisms of Carbon Dioxide and pH Effects on Metabolism Topics in Environmental Physiology and Medicine Carbon Dioxide and Metabolic Regulations Pages 107-117 Springer-Verlag New York.		N	Y		N	P	Applicant's reference number CO2 136	1974
Nahas GG, Steinsland OS	Increased Rate of Catecholeamine Synthesis During Respiratory Acidosis Respiration Physiology Vol 5, pages 108-117		N	Y		N	P	Applicant's reference number CO2 176	1968
Poyart C, Nahas GG	Inhibition of Catecholamine-Induced Calorigenesis and Lipolysis by Hypercapnic Acidosis Am J Physiol Vol 211 pages 161-168		N	Y		N	P	Applicant's reference number CO2 201	1966

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Rentokil Initial plc	Loss of Carbon Dioxide from Carbonated Drinks		N	N		Y	A	Applicant's reference number CO2 224	2003
Rentokil Initial UK Ltd	Safety Data Sheet for Carbon Dioxide dated 10/05/96 Issue 01			Y		N	P		1996
Richards JB, Stein SN	Effect of CO2 Exposure and Respiratory Acidosis on Adrenal 17-Hydroxycorticosteroid Secretion in Anesthetized Dogs Am J Physiol Vol 188 pages 1-6		N	Y		N	P	Applicant's reference number CO2 206	1957
Riley RL, Barnea-Bromberger B	Monitoring Exposure of Brewery Workers to CO2 : A Study of Cellar Workers and Controls Archives of Environmental Health Vol 34. Number 2 pages 92-96		N	Y		N	P	Applicant's reference number CO2 205	1979
Schaefer KE	Blood pH and pCO2 Homeostasis in Chronic Respiratory Acidosis Related to the Use of Amine and Other Buffers Annals New York Academy of Sciences Vol 92 Pages 401-412		N			N	P	Applicant's reference number CO2 108	1961

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Schaefer KE, McCabe N, Withers J	Stress Response in Chronic Hypercapnia American Journal of Physiology Vol. 214, No 3 Pages 543-548		N	Y		N	P	Applicant's reference number CO2 109	1968
Sechzer PH, Egbert LD, Linde HW, Cooper DY, Dripps RD, Price HL	Effect of CO2 Inhalation on Arterial Pressure, ECG and Plasma Catecholamines and 17-OH Corticosteriods in Normal Man J Appl Physiol Vol 15, pages 454-458		N	Y		N	P	Applicant's reference number CO2 131	1960
Stein SN, Lee RE, Annegers JH, Kaplan SA, McQuarrie DG	The Effects of Prolonged Inhalation of Hypernormal Amounts of Carbon Dioxide. 1 Physiological Effects of 3% CO2 for 93 days Upon Monkeys Research Report No. NM 240100.01.01 US Naval Research Institute, Bethesda Md.		N	Y		N	P	Applicant's reference number: CO2 142	1959
Tharr D	Carbon Dioxide Exposures to Medical Personnel as a Result of Wearing Surgical Isolation Suits Applied Occupational and Environmental Hygiene Vol 13 No 2 Pages 87-90		N	Y		N	P	Applicant's reference number CO2 273	1988

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
US Army Medical Research	Live Fire Support Services Expansion of the N Gas Model for Toxic Potency to Include NO2 Effects. Jaycor 2904-01		N	Y		N	P	Applicant's reference number CO2 98	1994
Vandemark NL, Schanbacher BD, Gomes WR	Alterations in Testes of Rats Exposed to Elevated Atmospheric Carbon Dioxide J Reprod. Fert Vol 28, pages 457-459		N	Y	Y	N	P	Applicant's reference number CO2 111	1972

Environmental Fate and Behaviour and Ecotoxicology

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Alabaster JS, Herbert DWM, Hemens J	The Survival of Rainbow Trout (Salmo gairdnerii Richardson) and Perch (Perca fluviatilis L.) At Various Concentrations of Dissolved Oxygen and Carbon Dioxide Annals of Applied Biology Vol 45(I) pages 177-188		N	Y	Y	N	P	Applicant's reference number CO2 125	1957
Anonymous	Fundamentals of Physical Geography. Introduction to Biogeography and Ecology The Carbon Cycle. www.geog.ouc.bc.ca/physgeog/contents/9r.html /			Y		N	P	Applicant's reference number CO2 216	2003
Battish SK, Kumari P	Effect of Physico-chemical Factors on the Seasonal Abundance of Cladocera in Typical Pond at Village of Raqba, Ludhiana Indian Ecol. 13 (1): 146 -151		N	Y		N	P	Applicant’s reference number CO2 276	1986

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Hamada Y, Tanaka T	Dynamics of Carbon Dioxide in Soil Profiles Based on Long-Term Field Observation Hydrological Processes 15, 1829-1845		N	Y		N	P	Applicant's reference number CO2 279.	2001
Huffman H	Minimum Ventilation www.gov.on.ca/OMAFRA/english/livestock/poultry/facts/min_vent.htm /			Y		N	P	Applicant's reference number CO2 215	2003
Jones J, Mulholland PJ	Influence of Drainage Basin Topography and Elevation on Carbon Dioxide and Methane Supersaturation of Stream Water Biogeochemistry 40: 57-72		N	Y		N	P	Applicant's reference number CO2 275	1988
Nielsen MG, Christian K, Birkmose D	Carbon dioxide concentrations in the nests of the mud dwelling mangrove ant Polyrhachis sokolova Forel (Hymenoptera: Formicidae) Australian Journal of Entomology 42, 357-362		N	Y		N	P	Applicant's reference number CO2 277	2003

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
Paul RJ, Colmorgen M, Pirow R, Chen YH, Tsai MC	Systemic and Metabolic Responses in Daphnia magna to anoxia Comparative Biochemistry and Physiology Part A 120, 519-530		N	Y		N	P	Applicant's reference number CO2 278	1988
Ross RM, Krise WF, Redell LA, Bennett RM	Effects of Dissolved Carbon Dioxide on the Physiology and Behaviour of Fish in Artifical Streams Environmental Toxicology Vol 16 pages 84-95		N	Y	Y	N	P	Applicant's reference number CO2 129	2001
Thompson BA, Harteck P, Reeves RR Jr	Ultraviolet Absorption Coefficients of CO2, CO, O2, H20, N20, NH3, NO, SO2 and CH4 between 1850 and 4000 A. Journal of Geophysical Research Vol 68, No. 24 Pages 6431-6436		N	Y		N	P	Applicant's reference number CO2 175	1963
Todar K	Physical and Environmental Requirements for Microbial Growth www.bact.wisc.edu/MicrotextBook/NutritionGrowth/physicalandenv.html /			Y		N	P	Applicant's reference number CO2 95	2002

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date
UK Home Office	The Humane Killing of Animals under Schedule 1 to the Animals (Scientific Procedures) Act 1986 Code of Practice The Stationery Office Limited			Y	Y	N	P	Applicant's reference number: CO2 139	1986
Zaller JG, Arnone III, JA	Activity of surface-casting earthworms in a calcareous grassland under elevated atmospheric CO2. Oecologica Vol 111 pages 249-254		N	Y		N	P	Applicant's reference number CO2 212	1997

Classification and Labelling

Author	Title	Laboratory	GLP/GEP Study Y/N	Published Y/N	Vertebrate Study Y/N	Data Protection Claimed Y/N	Data Owner[11]	Report No. / Study ID	Report Date