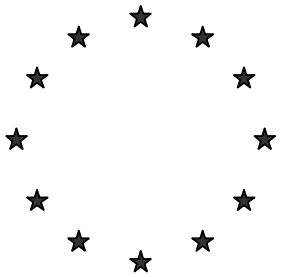
Directive 98/8/EC concerning the placing biocidal products on the market

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

Assessment Report



Carbon Dioxide

Product-type 18
(Insecticides, Acaricides and Products to control other Arthropods)

May 2010

Annex I - France

Carbon dioxide (PT 18)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 27th May 2010 in view of its inclusion in Annex I 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 18 (insecticide), 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 and 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 18.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[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 7(1) 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 18 was 30 April 2006, in accordance with Article 9(2) of Regulation (EC) No 1451/2007.

On 25 April 2006, 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 25 July 2006.

On 19 February 2008, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 17 March 2008. The competent authority report included a recommendation for the inclusion of carbon dioxide in Annex I to the Directive for product-type 18.
In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the competent authority report publicly available by electronic means on 24 March 2008. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.
In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Commission.

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 Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

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 the Annex I of Directive 98/8/EC and consulted the Standing Committee on Biocidal Products on 27th May 2010.
In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 27th May 2010.

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 the Annex I of Directive 98/8/EC for product-type 18. The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product-type 18 that contain carbon dioxide. 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 this 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 there are products containing carbon dioxide for the product-type 18, which will fulfil the requirements laid down in Article 5 of Directive 98/8/EC. This conclusion is however subject to:

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

ii. the implementation of the provisions of Article 5(1) of Directive 98/8/EC, and

iii. the common principles laid down in Annex VI to Directive 98/8/EC.

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 product authorisation 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 to Directive 98/8/EC.

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

2 OVERALL SUMMARY AND CONCLUSIONS

2.1 General substance information / general product information

Carbon dioxide has been evaluated for its use as insecticide (product type 18). In this use as a fumigant insecticide, pure carbon dioxide is applied from a gas cylinder into a fumigation bubble to a level of at least 60% v/v. As a fumigant insecticide, carbon dioxide is intended for use by professional operators.

2.2 Identity of the active substance

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 at concentrations of 99-100% but the method was not validated at lower concentrations.
It has not been considered necessary to submit analytical methods in environmental matrices because the exposure assessment has shown that the use of carbon dioxide as insecticide should not cause any increase of carbon dioxide concentrations outside natural range in water (including groundwater), sediment or soil.
Analytical methods in animal and human body fluids and tissues were not considered as mandatory in view of the toxicological properties of the substance, although generic information has been provided. Similarly, analytical methods in food and feedstuff were not deemed necessary because of the nature of carbon dioxide.

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.

2.3 Physico-chemical properties

Carbon dioxide is a colourless and odourless gas under normal temperature and pressure conditions with a molecular mass of 44.01 g/mol and a relative density of 1.527. It is soluble in water (88 ml carbon dioxide in 100 ml water) and soluble in isobutanol and cyclohexanol. Its partition coefficient (log Kow) between octanol and water was calculated as 0.83. In water, dissolved carbon dioxide will form carbonic acid and subsequently bicarbonate and carbonate ions. Both reactions are reversible and lead to equilibrium depending on the pH. Thermodynamically, carbon dioxide is stable under normal pressure up to approximately 300°C. Over this temperature, it dissociates into carbon monoxide and oxygen. At normal temperature, CO_2 is stable from 10^{-5} to 100 atm. Carbon dioxide is neither flammable nor explosive and has no oxidising properties.

2.4 Classification and labelling

2.4.1 Existing classification and labelling

Non hazardous according to the Directive 67/548/EC.

2.4.2 Proposal for labelling

No critical end points in terms of adverse health or environmental effects or physico-chemical properties have been identified for carbon dioxide. These findings are consistent with its classification for supply under directive 67/548/EEC replaced by regulation 1272/2008 CE, as non-hazardous for health, the environment and physical-chemical effects. It is proposed that this classification remains unchanged.

Classification	None (non hazardous)
Class of danger	None (non hazardous)
R phrases	None (non hazardous)
S phrases	None (non hazardous)

2.5 Efficacy and intended uses

Carbon dioxide is an insecticide for use by professional operators for the control of Dictyoptera (cockroaches), Coleoptera (beetles), Lepidoptera (butterflies and moths), Psocoptera (booklice), Acari (mites) and Hemiptera (bugs) in public hygiene and food storage premises (other than uses falling within the scope of regulation EC n°1107/2009 on the placing on the market of plant protection products). In its application as a fumigant insecticide, 20 studies have demonstrated a sufficient degree of efficacy across all life stages. Within a fumigation bubble, carbon dioxide levels are maintained at a minimum concentration of 60% v/v. Some efficacy studies demonstrate 100% mortality after only one day, but to ensure that 100% mortality is achieved, a minimum of three days is stipulated for the fumigation period, the extension of 4 to 6 weeks is applied in the same way. Mortality of insects will be achieved between 3 days and 6 weeks, depending upon insect species present.

Subtle physiological effects due to elevated carbon dioxide levels are increased use of oxygen (i.e. respiration), reduced fecundity and reduced life span of adults. Consequently, some states of insects (i.e. diapausing larvae) were shown to be more tolerant to CO2 as they exhibited lower respiration rates. Carbon dioxide seems to exert its anaesthetic effect directly on the nervous system via the trachea and not via the blood. In experiments with locusts and ^{14}C-labelled carbon dioxide, ^{14}C was detected in all insect body parts, but its relative persistence was highest (up to 24 hr) in the central nervous system or its immediate vicinity. Pure carbon dioxide has an inhibitory effect on the bioelectrical responses of the nervous system, while a smaller concentration (15%) has a stimulatory effect. Carbon dioxide has also been reported to induce depolarisation of the neurons.

Most insects respire by means of a tracheal system. In this system, gas is directly transported to the tissues by air-filled tubules that bypass blood. The pores to the outside, called spiracles, deliver the gases of respiration. The drawback of this system is that the gases diffuse slowly in the long narrow tubules; as a result, these tubes need to be limited in size for adequate gas transfer. The advantage is that oxygen and carbon dioxide diffuse much faster (10,000 times faster), from the air than in water, blood or tissues. Unlike in mammals however, there is uncertainty as to whether the actions of carbon dioxide on insects result from a specific effect of this agent, from anoxia (reduced oxygen levels), and/or pH variations (Ref A5.4/01). What is known, is that with increasing levels of carbon dioxide, narcosis will occur, followed ultimately by death (Ref A5.4/2).

Resistance to carbon dioxide is unlikely to occur because, when used as a biocide, it will be lethal to the target insects in a single dose (as demonstrated by the information submitted for the representative insecticide product containing carbon dioxide). This means that there is no mechanism for resistance to carbon dioxide to develop because target organisms are never exposed to sub-lethal concentrations of carbon dioxide (as a biocide). Given the fact that resistance to carbon dioxide cannot develop because of the way it is used (see above), a management strategy for the control of the development of resistance to carbon dioxide has not been proposed.

Carbon dioxide can be used as a biocide in public hygiene situations for the treatment of a variety of non-food products including Packaging materials, Transport containers, Food processing machinery, Manufactured goods, Textiles, etc. No specifications about the maximum size of the bubble were presented in the dossier: It must be noted that there are practical limits on the size of the bubble and the amount of CO2 required, and a bubble greater than 5 x 5 x 5 metres is unlikely. The usual size is approximately 3 x 3 x 3 metres. A fumigation bubble will either be a single use chamber made up on site from plastic coated foil, or a reusable prefabricated chamber made from PVC coated polyester fabric (Specifications for both materials can be found as references B5.2/01 and B5.2/02, but no specifications about maintenance procedures in general and especially cleaning procedures, airtightness control, and use-by date were provided). Carbon dioxide gas is delivered into the fumigation bubble until a minimum concentration of 60% v/v carbon dioxide is achieved. These levels are checked periodically and maintained throughout the treatment period. The optimum temperature used for the fumigation is 25°C. The length of a fumigation treatment will be determined primarily by insect species present and ambient temperature and will typically be between 3 days and 6 weeks. At the end of the treatment, carbon dioxide is pumped out of the fumigation bubble direct to the outside atmosphere and once levels have reached a suitable level, below the workplace exposure limit of 0.5%, the bubble is dismantled and contents removed.

2.6 Toxicological assessment

2.6.1 Hazard identification and effects assessment

In this dossier, a justification for non submission of data was provided 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 context of the representative biocidal product, the fumigation bubble. Accordingly, exposures via the oral and dermal route were not considered further.

- 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.

↳ One of the most recursive justifications for non submission of data is based on the low exposure potential of the substance during its use. This justification was not fully accepted by the RMS in view of the results of the exposure assessment.

↳ There is a sufficient database of information available on carbon dioxide. This database gives a coherent toxicological profile of the substance.

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

The information submitted shows that 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% (20,000-30,000 ppm) (v/v) CO_2, panting and tachycardia at 5-6% (50,000-60,000 ppm), to respiratory and heart distress and loss of consciousness at 10% (100,000 ppm) and finally death if the exposure is not quickly stopped. These effects are linked with respiratory acidosis.

Toxicity to fertility (morphological changes of spermatozoa in mice at 35% (350,000 ppm) and testicular changes in rats at 2.5% (25,000 ppm)) and teratogenicity (cardiac and skeletal abnormalities in rats at 6% (60,000 ppm); skeletal abnormalities in rabbits at 10% (100,000 ppm)) were also observed. For that kind of effect, the mechanism of action is uncertain.
This point has been discussed in PT14, and it has been concluded that based on the human general toxicity and the lack of human information available on teratogenicity, the limited evidence in animal 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.

The 5,000 ppm (0,5%) concentration (WEL[4] for safe working conditions given in 2006/15/EC European directive in application of the 98/24/EC) has been chosen for the risk assessment. For the specific case of CO2, for which the human metabolism is well known, 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. For the purpose of the risk assessment, this WEL should be considered as an AEL[5]. For the same reason, because the WEL value was accepted at the EU level, justifications for non submission of data were accepted and new testing was not deemed necessary on carbon dioxide.

2.6.2 Exposure assessment

➢ Production

Using the appropriate engineering controls (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

[4] Workplace Exposure Level.

[5] AEL: Acceptable Exposure Level

carbon dioxide levels never increase above the established maximum occupational exposure limit.

➢ Professional users

No specifications about the maximum size of the bubble were given, or on the size of the surrounding room. In the absence of precise data, a formal quantitative risk assessment cannot be performed, and therefore the risk characterisation had to focus on protective equipment and safety measures.
The applicant provided no maximum size of the bubble because bubble size has to be adapted to the object to be treated and can be variable. It must be noted however that, according to the applicant, there are practical limits on the size of the bubble and the amount of CO2 required, and a bubble greater than 5 x 5 x 5 metres is unlikely. The usual size is approximately 3 x 3 x 3 metres.

Measurements of operator exposure to carbon dioxide during fumigation activities have been provided for the 3 main tasks during which the operator may be exposed to the active substance (filling the fumigation bubble, monitoring CO_2 levels in bubble, venting). The greater exposure was measured during venting, for which an average value of about 3,820 ppm (0.38 %) was recorded[6].
During these experiments, CO_2 concentrations, measured with diffusion tubes, are averaged on a 1-hour basis. This method is not very sensitive and transient peaks of carbon dioxide may not have been identified. For this reason, the averaged values derived from these exposure measurements should be considered with caution, as they may not reflect the maximum exposure concentrations.
The applicant has indicated that fumigators wear personal electrochemical detectors during all the fumigation process. When the concentration is above 5,000 ppm (0.5 %) an alarm sounds and the fumigators have to wear appropriate equipment such as Self-Contained Breathing Apparatus (SCBA). Alternatively, Escape Self Contained Breathing Apparatus (ESCBA)[7] can be proposed as being much less heavy than SCBA and more convenient but are only suitable for escape in case of quick increase of the CO_2 level in the fumigation area due to the very low autonomy of this apparatus. The appropriateness of the equipment will have to be evaluated depending of the conditions of uses. According to the manufacturer of personal electro-chemical detectors, CO_2 levels are almost instantaneously detected, thus ensuring an adequate alert system for the fumigator[8]. In these conditions, provided detectors are worn, operator exposure should not be higher than 5,000 ppm (0.5 %) and this concentration was proposed by the applicant to be the realistic worst case for both short term and long term exposure in all the fumigation process.

[6] The RMS draws the attention of other MS on the fact that this value should be handled as an example of a situation which may not be representative of standard conditions since no specifications about the bubble volume compared to the room volume were provided.

[7] ESCBA according to EN 402.

8 It is agreed that other detection system can be used provided they can demonstrate a sufficient sensitivity and are suitable to detect transient levels of CO_2.

➢ Bystanders

All such fumigations are carried out in unoccupied premises. Persons not involved, be they adults or children, are not allowed to enter the designated risk area until the fumigator in charge has issued a "certificate of gas clearance". This is only issued after the fumigation bubble has been ventilated and once background levels of carbon dioxide have fallen below 1,000 ppm (0.1 %).

In addition, it should be noted that once a fumigation bubble is vented there are no residues of carbon dioxide remaining as all is dispersed to atmosphere.

➢ Non-professional exposure

This product is intended for use only by professional operators. Primary exposure to non-professional users has therefore not been considered. Nevertheless, based on the specificity of the conditions of use of carbon dioxide for fumigation applications, and the risk mitigation measures already needed for professional users, it is recommended to limit the use to professional users only.

2.6.3 Risk characterisation

➢ Production

Information has been provided indicating that using the appropriate engineering controls (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. Within the framework of the Biocide Product Directive, information is deemed acceptable.

➢ Professional users

From its use as a fumigant insecticide, professional users could potentially be exposed to large quantities of carbon dioxide. As carbon dioxide is a gas, the route of exposure would be via inhalation.

An operator exposure study was carried out in which two fumigators wore carbon dioxide detector tubes on their person (filling the fumigation bubble, monitoring CO_2 levels in bubble, venting). Three different operations were identified where it was considered that there was a possibility of exposure to the fumigators. All the measurements recorded were below both the long-term Workplace Exposure Limit (WEL) 0.5 % (5,000 ppm) and the short-term WEL 1.5 % (15,000 ppm). However, in the worst case, the calculated % AEL is very close to 100 %, for the task "venting at the end of the fumigation process" (87.3 %).

This high % AEL considered together with the low sensitivity of the method of analysis during the experiment does not provided sufficient proof that an acceptable risk can be achieved.
As a complement to the risk assessment, the applicant has stated that fumigators have to be equipped with personal electro-chemical detectors and that if carbon dioxide levels were ever to rise above 5,000 ppm (0.5 %), an alarm would sound. It is in these instances that Self Contained Breathing Apparatus (SCBA) would be used to allow exit from the Risk Area until acceptable safe working levels (i.e. < 0.5%) have been attained.

Due to the rapid action of carbon dioxide, this precaution seems to be insufficient to protect the operator. In fact, it cannot be excluded that Self Contained Breathing Apparatus may be out of reach when the alarm would sound. In addition, despite the sensitivity claimed by the manufacturer of the personal electro-chemical detectors, it cannot be ascertained that some exposure to carbon dioxide has not already taken place before the alarm rings. For this reason, RMS recommends the use of appropriate equipment such as Self Contained Breathing Apparatus (SCBA) for each task specified above.

Appropriate equipment such as Self Contained Breathing Apparatus (SCBA) must be used until acceptable safe working levels (i.e. < 0.5 %) has been attained and until the end of the fumigation process (end of venting the bubble).

Alternatively, Escape Self Contained Breathing Apparatus (ESCBA)[9] with wearing electrochemical portable detector can be proposed as being much less heavy than SCBA and more convenient but are only suitable for escape in case of quick increase of the CO_2 level in the Risk Area due to the very low autonomy of this apparatus. The appropriateness of the equipment will have to be evaluated depending of the conditions of uses.

Taking these factors into account, the use of carbon dioxide as a fumigant insecticide by operators does not present an adverse inhalation risk, provided that the alarm device is relevant and if the operators wear an *ad hoc* personal protective equipment.

- By-standers

All such fumigations are carried out in unoccupied premises. Persons not involved, be they adults or children, are not allowed to enter into the designated risk area until the fumigator in charge has issued a “certificate of gas clearance”. This is only issued after the fumigation bubble has been ventilated and once background levels of carbon dioxide have fallen below 0.1 % (which is below the long term WEL of 0.5 % (5,000 ppm)).

[9] ESCBA according to EN 402.

2.7 Environmental assessment

The environmental section of the carbon dioxide dossier is reduced, mainly due to the nature of the active substance "carbon dioxide", naturally occurring and omnipresent in the environment, and to the low environmental exposure to the substance used as insecticide.

2.7.1 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 following:

- 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…), etc…).

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, these 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.

2.7.2 Environmental exposure assessment

The exposure assessment shows that it is especially during the venting process of a fumigation bubble that carbon dioxide is sent directly to the outside air compartment. The fumigation bubble contains a minimum level of 60 % v/v of carbon dioxide. Due to its nature as a gas, the carbon dioxide is expected to be rapidly and readily dispersed and immediately diluted into the surrounding air. The room is also likely to have some airflow, which will help to dissipate the carbon dioxide. Thus the rapid dispersal of carbon dioxide following venting, carbon dioxide as fumigant insecticide is not expected to increase significantly the indoor air concentrations, and subsequently is not expected to increase significantly the local environmental concentrations of carbon dioxide.
In addition, considering the European tonnage involved in the use of carbon dioxide as insecticide compared to the natural burden of carbon dioxide in the atmosphere (about 800 gigatons of carbon in the atmosphere) or the current annual release of carbon dioxide due to other anthropogenic activities, it is unlikely that the use of carbon dioxide as an insecticide will significantly affect the atmosphere concentration outside normal atmospheric ranges
Consequently:

- There will be no significant exposure of the aquatic environment to carbon dioxide. Consequently, adverse effects to aquatic organisms and sediment dwelling organisms from the use of carbon dioxide as insecticide do not need to be considered.

- The use pattern proposed for the biocidal product in fumigation bubbles, 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 insecticide.

The PEC was set at zero for all the compartments, meaning that the use of carbon dioxide as a biocide in fumigation bubbles will not increase carbon dioxide concentrations outside natural range.

2.7.3 Risk characterisation

Given the particular nature of carbon dioxide and its natural occurrence in the environment and the low level of exposure expected in all environmental compartments from the use of carbon dioxide as an insecticide, it has been concluded that there is no risk to the environment or wildlife.

In view of the fate and behaviour of carbon dioxide in the water compartment, notably the equilibrium of carbon dioxide and carbonate in water, and the low level of exposure expected from its use as insecticide, no risk for drinking water or groundwater has been identified.

Due to the particular nature of carbon dioxide, it has to be considered that carbon dioxide does not fulfil persistence criteria in any environmental criteria and has no bioaccumulation potential.
Carbon dioxide has no PBT potential.

2.8 Summary of the risk assessment

Carbon dioxide has been evaluated for its use as a fumigant insecticide (product type 18). In this use as a fumigant insecticide, pure carbon dioxide is applied from a gas cylinder into a fumigation bubble to a level of at least 60 % v/v. As a fumigant insecticide, carbon dioxide is intended for use by professional operators only and so exposure to the general public will not occur during its normal use. The only possible exposure to consumers might be indirect, secondary exposure, and yet this is highly unlikely as a result of the procedures in place when carrying out such a treatment.

The principle 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 context of the representative biocidal product. Accordingly, exposures via the oral and dermal routes have not been considered further. No critical endpoints in terms of adverse health effects or physical-chemical properties have been identified for carbon dioxide, and these findings are consistent with its classification for supply as non-hazardous for health and physical-chemical effects.

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, there is air monitoring at the plant to ensure carbon dioxide levels never increase above the established maximum occupational exposure limit for safe working conditions (0.5 %, or 5,000 ppm or 9150 g/m^3, 8 hour time weighted average). There is no separate manufacturing process for the carbon dioxide used as a fumigant insecticide by Rentokil Initial.

It has been concluded that the engineering controls intrinsic in carbon dioxide production, together with operator training and the availability of personal protective equipment (PPE) ensure there is minimal risk of exposure of workers to carbon dioxide.

Under normal conditions of use, levels of carbon dioxide that operators are exposed to, have been seen to be below both the long term and short term WELs (5,000 ppm (0.5 %) and 15,000 ppm (1.5 %) respectively).

Of the three different procedures within a fumigation operation (filling the fumigation bubble, monitoring CO_2 levels in bubble, venting), venting of the bubble at the end of the fumigation process, poses the greatest risk, giving in the worst case a 87.3 % AEL.
This high % AEL considered together with the low sensitivity of the method of analysis during the experiment does not provided sufficient proof that an acceptable risk can be achieved.
Appropriate equipment such as Self Contained Breathing Apparatus (SCBA) must be used until acceptable safe working level (i.e. < 0.5 %) has been attained and until the end of the fumigation process (end of venting the bubble).
Alternatively, Escape Self Contained Breathing Apparatus (ESCBA)[10] can be proposed as being much less heavy than SCBA and more convenient but are only suitable for escape in

[10] ESCBA according to EN 402.

case of quick increase of the CO_2 level in the fumigation area due to the very low autonomy of this apparatus. The appropriateness of the equipment will have to be evaluated depending of the conditions of uses.
The product is not intended to be used by non-professional users.
All such fumigations are carried out in unoccupied premises. Persons not involved, be they adults or children are not permitted entry into the designated risk area until the fumigator in charge has issued a "certificate of gas clearance". This is only issued after the fumigation bubble has been ventilated and once background levels of carbon dioxide have fallen below 1,000 ppm (0.1 %).

As carbon dioxide is thermally stable, non-flammable, non-explosive and non-oxidising there is no risk to professional users from its **physical-chemical properties**. This is also the case for carbon dioxide used as a fumigant insecticide.

The use pattern of carbon dioxide as a fumigant insecticide, and the fact that it is a gas means that there will be no significant exposure to livestock and pets via drinking water or feeding stuffs.

A semi-quantitative risk assessment was conducted for the **environment**. Under normal conditions of use, there will be no exposure of carbon dioxide to the aquatic environment. This indicates that no adverse effects to aquatic organisms and sediment dwelling organisms from the use of carbon dioxide as a fumigant insecticide are expected. The use pattern proposed means that carbon dioxide will not enter sewage treatment plants and therefore adverse effects on micro-organisms in sewage treatment plants are not expected either.
Similarly for the atmospheric compartment, the quantities of carbon dioxide involved for the use as an insecticide indicates that there will be no increase in the levels of carbon dioxide outside normal atmospheric ranges. The risk for biotic or abiotic adverse effects is deemed acceptable.
No significant increase of carbon dioxide concentrations in the atmosphere from the use of carbon dioxide as a fumigant insecticide is anticipated, and therefore no risk were identified for the terrestrial compartment.
No concerns were identified for carbon dioxide with regards to:

- Persistency in soil or water
- Groundwater and drinking water contamination
- Bioaccumulation (carbon dioxide does not fulfil PBT criteria)
- Non compartment specific effects relevant to the food chain (secondary poisoning)

Given the very low level of exposure expected of all environmental compartments from the use of carbon dioxide as a fumigant insecticide, it has been concluded that there is no risk to the environment or wildlife.

3 DECISION

3.1 Background to the Decision

The carbon dioxide dossier has been submitted for its use as an insecticide in a fumigation bubble. The evaluation has been carried out for the uses as specifically described by the applicant: Carbon dioxide is intended for use by professionals only.

On the basis of the proposed and supported uses and the evaluation conducted as summarised in Sections 2.1-2.8, the evaluation of the dossier led to the following conclusions concerning carbon dioxide as insecticide in fumigation bubbles:

- The substance is correctly identified with a purity > 99 % (v/v). No additive or impurity is above the concentration limit of 1 g/kg.
- The physical-chemical properties of the active substance have been determined and deemed acceptable for the purposes of the appropriate use, storage and transport of the active substance.
- Carbon dioxide is an insecticide for use by professional operators for the control of Dictyoptera (cockroaches), Coleoptera (beetles), Lepidoptera (butterflies and moths), Psocoptera (booklice), Acari (mites) and Hemiptera (bugs) in public hygiene and food storage practice. Mortality of insects will be achieved between 3 days and 6 weeks, depending upon insect species present.

  Examples of the species to be controlled include the following:

Acarus siro	Flour mite
Anastrephus suspensa	Caribbean fruit fly
Anobium punctatum	Common furniture beetle
Anthrenus verbasci	Varied carpet beetle
Blatella germanica	German cockroach
Callosobruchus chinensis	Cowpea weevil
Cimex lectularius	Bed bug
Dermestes maculatus	Leather beetle
Ephestia cautella	Tropical warehouse moth
Lasioderma serricorne	Cigarette beetle
Lepinotus patruelis	Booklouse
Liposcelis bostrychophilus	Booklouse
Oryzaephilus mercator	Merchant grain beetle
Oryzaephilus surinamensis	Saw-toothed grain beetle
Periplaneta americana	American cockroach
Plodia interpunctella	Indian-meal moth
Ptinus tectus	Australian spider beetle
Sitophilus granarium	Grain weevil
Sitophilus oryzae	Rice weevil
Sitotroga cerealella	Angoumois grain moth
Tribolium castaneum	Rust red flour beetle
Tribolium confusum	Confused flour beetle
Trogoderma glabrum	Warehouse beetle
Trogoderma granarium	Khapra beetle
Tyrophagus putrescentiae	Mould mite

  Without data supporting the efficacy of CO2 against *Ephestia keuhniella* (Mediterranean flour moth), it was not possible to maintain this target species in the dossier.
- The evaluation has used the existing operator exposure level for carbon dioxide set by various national bodies. The long-term workplace exposure limit for carbon dioxide

set in 2006/15/EC European directive in application of the 98/24/EC, is 5,000 ppm / 0.5 % (8 hour time weighted average while the short term workplace exposure limit is 15,000 ppm / 1.5 % (15 minutes reference period)).

- The conclusion of the toxicological assessment is that of the three different procedures within a fumigation operation, venting at the end of the fumigation process, poses the greatest risk for professional users, giving in the worst case an AEL of 87.3 %. In relation with the high AEL % and the limited confidence in the concentrations measured during human exposure experiments, Self Contained Breathing Apparatus (SCBA) must be used during the most dangerous steps of the fumigation process (filling and flushing the bubble) and when professionals enter in the fumigation area until the end of the process (end of flushing the bubble). Moreover in the case of a concentration above the acceptable safe working levels (i.e. < 0.5 %), the SCBA must be used until safe level has been attained. The SCBA used is suitable for the operation of fumigation with CO_2 but is not very convenient (heavy), thus RMS proposes to use hood or full face mask with compressed airline. As proposed by the applicant RMS recommend the wearing of personal electro-chemical detectors during all the fumigation process. Alternatively, Escape Self Contained Breathing Apparatus (ESCBA)[11] can be proposed as being much less heavy than SCBA and more convenient but are only suitable for escape in case of quick increase of the CO_2 level in the fumigation area due to the very low autonomy of this apparatus. The appropriateness of the equipment will have to be evaluated depending of the conditions of uses.
- The ecotoxicological assessment shows that environmental natural concentrations are not affected by the use of carbon dioxide as insecticides and there are no critical endpoints in terms of adverse ecotoxicological effects. The evaluation has concluded that under the proposed normal conditions of use, there are no unacceptable effects on the environment or wildlife, as provided for in Article 5 (1) (b) (iv) of Directive 98/8/EC provided certain conditions are taken into account as detailed in sections 2.1 and 2.2 of this report.
- 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.
- It must be noted that carbon dioxide is used for control of arthropod pests that affect commodities, such as; museum artefacts (wooden items, textiles, etc), etc. It is particularly important for very high value commodities such as certain museum artefacts, which may be adversely affected by other fumigants. While normally treatment of wooden artefacts (frames of “old masters”) would require PT8 inclusion, it seems appropriate to limit the inclusion to PT18 on account of the limited and specialised use of carbon dioxide.

3.2 Decision regarding Inclusion in Annex I

On the basis of the proposed and supported uses and the evaluation conducted as summarised in Section 2, it can be concluded that the proposed use of carbon dioxide under specified conditions fulfils the safety requirements laid down in Article 5(1) (b), (c) and (d) of Directive 98/8/EC. This conclusion is, however, subject to compliance with the particular requirements described in this report.

[11] ESCBA according to EN 402.

In view of the above, it is concluded that carbon dioxide shall be included in Annex I of Directive 98/8/EC as an active substance for use in product-type 18 (insecticides), subject to the following specific provisions:

- The active substance, as manufactured, shall have a minimum purity of 990 mL/L.
- Product may only be sold to and used by professionals trained to use them.
- Appropriate measures to protect operators shall be taken to ensure minimum risk, including the availability of personal protective equipment if necessary.
- Appropriate measures shall be taken to protect bystanders, such as exclusion from the treatment area during fumigation..

Primary exposure to non-professional users has not been considered in the application for Annex I inclusion submitted because the reference product was only foreseen for professional users. Nevertheless, based on the specificity of the conditions of use of carbon dioxide for fumigation applications, and the risk mitigation measures already needed for professional users, it has been decided to restrict the use to professional users only.

Extension of the use pattern beyond those reviewed will require a re-evaluation of the Annex I entry of carbon dioxide in order to establish whether the proposed extensions can satisfy the requirements of Article 10(1).

In order to facilitate the work in the Member States in granting or reviewing authorisations 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 I.

3.3 Decision regarding Inclusion in Annex IA

The applicant asked consideration to be given for inclusion of carbon dioxide in Annex IA.

In view of the high AEL % for the applicator and the need of specific personal protective equipment, it is concluded that carbon dioxide shall not be included in Annex IA of Directive 98/8/EC as an active substance for use in product-type 18 (insecticides).

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

- Product may only be sold to and used by professionals trained to use them, and measures shall be taken in order to prevent carbon dioxide concentrations in the Risk Area from reaching the level that was established as the short-term occupational exposure limit.

- Appropriate breathing apparatus such as Self Contained Breathing Apparatus (SCBA) or hood or full face mask with compressed airline must be used when professionals enter in the fumigation area until the end of the process (end of flushing the bubble). At the end of the process, the SCBA must be used until a concentration under the acceptable safe working levels (i.e. < 0.5%) has been attained. Alternatively, Escape

Self Contained Breathing Apparatus (ESCBA)[12] can be proposed as being much less heavy than SCBA and more convenient but are only suitable for escape in case of quick increase of the CO_2 level in the fumigation area due to the very low autonomy of this apparatus. The appropriateness of the equipment will have to be evaluated depending of the conditions of uses.

- The use of the fumigation bubble has not been assessed in areas where contact with food or feedstuffs was anticipated. Despite this indication, Member States are invited to ensure that the appropriate requirements are fulfilled should any national application for authorisation concerns a use where contact with food or feedstuffs may occur.

3.5 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 in Annex I of the Directive 98/8/EC.

However, the limit of quantification for the analytical method submitted has not been provided. Member States shall ensure that the appropriate methods of analysis are made available before any placing on the market.

3.6 Grounds for comparative assessment

The intended normal uses and properties of carbon dioxide and the consequent risks to health or the environment which give rise to concern have been reviewed in order that comparative assessment can be done later, if necessary. Based on this evaluation, no areas of concern have currently been identified which would justify choosing carbon dioxide as a candidate for comparative assessment. The levels of exposure expected from the use of carbon dioxide as a fumigant insecticide, and its general low hazard in the use pattern identified contribute to this conclusion.

3.7 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.

[12] ESCBA according to EN 402.

APPENDIX I: LIST OF ENDPOINTS

Active substance (ISO Common name)	Carbon dioxide
Function (*e.g.* fungicide)	Insecticide

Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

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 (at 760 mmHg). 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 cyclohexanol or 1.2 g/l at 26°C)
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.

Classification and proposed labelling

with regard to physical/chemical data	Not classified as hazardous.
with regard to toxicological data	Not classified as hazardous.
with regard to fate and behaviour data	Not classified as hazardous.
with regard to ecotoxicological data	Not classified as hazardous.

Chapter 2: Methods of analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	Two methods are used: The Asco method and Infrared analyser method. Principles of the Asco method: A known volume of the test gas is isolated in a gas burette and treated with Potassium Hydroxide solution. The carbon dioxide dissolves leaving a bubble of residual gases which are left in the measuring section of the burette, where its volume is read off. Principles of the infrared analyser method: The infrared analyser measures the total carbon dioxide level of the test gas in comparison to a "zero gas" (which contains 100% carbon dioxide).
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	Not applicable. There are no additives present in carbon dioxide. There are no impurities present in carbon dioxide above the concentration limit of 1g/kg, and no impurities of toxicological or ecotoxicological significance present below the concentration limit of 1g/kg.

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	No analytical method has been submitted. This is because the environmental risk assessment shows that carbon dioxide, when used as a biocide, does not enter the soil compartment because there is no mechanism for the carbon dioxide to be released directly into the soil compartment.
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Given that carbon dioxide is a gas, the analytical method specified for the technical active substance (above) is suitable for detecting carbon dioxide in air.
Water (principle of method and LOQ) (Annex IIA, point 4.2)	No analytical method has been submitted. This is because the environmental risk assessment shows that carbon dioxide, when used as a biocide, does not enter the aquatic environment. This means that the use of carbon dioxide, when used as a biocide, does not affect the levels of carbon dioxide found naturally in the environment, outside normal atmospheric levels.
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Not applicable because carbon dioxide is not classified as hazardous.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Carbon dioxide fumigations are carried out on certain foodstuffs and it should be noted that carbon dioxide is generally recognised as a safe food substance (GRAS). In 1981, the Environmental Protection Agency in the USA waived the need for data requirements pertaining to toxicological studies, metabolism studies, analytical methods and residue data. The final ruling was given as follows: The food additive

	carbon dioxide may be safely used after harvest in modified atmospheres for stored product insect control on all processed agricultural commodities.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Not applicable.

Chapter 3: 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 normal use of carbon dioxide in Rentokil Initial's fumigant insecticide product 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).
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 normal use of carbon dioxide in Rentokil Initial's insecticide fumigant 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 normal use of carbon dioxide in Rentokil Initial's insecticide fumigant 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 normal use of carbon dioxide in Rentokil Initial's insecticide fumigant 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 given in 2006/15/EC European directive in application of the 98/24/EC 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)* *See footnote.
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)* *See footnote.

*Footnote

Existing data on the subchronic toxicity of carbon dioxide are available, including data on man. However, it is acknowledged that this data, (which is summarised in Document IIIA Section 6.4.3 of the Competent Authority Report) 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 an insecticide

fumigant 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.
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.* (*See footnote). However, it should be noted that the risk assessment for human health shows that the normal use of carbon dioxide in Rentokil Initial's insecticide fumigant products does not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges.

*Footnote
Refer to Document IIIA Section 6.6.1, 6.6.2, 6.6.3 and 6.6.4 of the Competent Authority Report, for the discussion about technically possibility to submit genotoxicity studies for carbon dioxide.

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 insecticide fumigant products does not cause any elevation of carbon dioxide in air, outside normal atmospheric ranges. 2. The normal working practices of carbon dioxide as an insecticide fumigant are within a sealed enclosure (fumigation bubble) and therefore additional exposure to the gas is not expected. 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 insecticide fumigant 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 effects 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.

*Footnote

Refer to Document IIIA Section 6.7 of the Competent Authority Report for full justification about why it is not scientifically necessary to determine the carcinogenic potential of carbon dioxide.

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 insecticide fumigant 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.

<u>* Footnote</u>

Refer to Document IIIA Section 6.8.1 of the Competent Authority Report for full justification about why these studies can be used to support the teratogenic assessment of carbon dioxide.

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.

<u>Other toxicological studies</u>

There is a substantial volume of data available on the toxicity of carbon dioxide, and none of it indicates that carbon dioxide is of sufficient concern to justify further investigation by a mechanistic study, or by routes of administration that are not considered in the core toxicity data set. In addition, carbon dioxide is not mixed or added to any other chemicals during it's normal use so it is not necessary to provide data on degradation products, by-products and reaction products relating to the human exposure to carbon dioxide.

Carbon dioxide fumigations are carried out on certain foodstuffs and it should be noted that carbon dioxide is generally recognised as a safe food substance (GRAS).

In 1981, the Environmental Protection Agency in the USA waived the need for data requirements pertaining to toxicological studies, metabolism studies, analytical methods and residue data.

The final ruling was given as follows: The food additive carbon dioxide may be safely used after harvest in modified atmospheres for stored product insect control on all processed agricultural commodities.

Carbon dioxide is also not intended for use directly on plants, making it unnecessary to consider the toxic effect of metabolites from treated plants.

Medical data

Effects of excessive carbon dioxide exposure in man are well reported in the product literature. These studies have been summarised in Document IIIA Section 6.1.3, 6.4.3, 6.5 and 6.12 of the Competent Authority Report. 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 insecticide fumigant (PT18) 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, the fumigation bubble.

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)	The long-term occupational exposure limit for carbon dioxide given in 2006/15/EC European directive in application of the 98/24/EC 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.		

Chapter 4: 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	In water: $CO_2 + H_2O \leftrightarrow H_2CO_3$
Ka_{oc}, Kd_{oc}	No soil specific data.
pH dependence	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)

Chapter 5: 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 INTENDED USES

Object and/or situation	Member State or Country	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks
				Type	Conc. of a.s.	Method kind	Number min max	Intervals between applications (min)	g as/L min max	water L/m^2	g as/m^2 min max	
Insects	All European countries	Controlled Atmosphere Technology / CO_2 Fumigation Bubble	The pest organisms to be controlled include the following insect orders: Dictyoptera (cockroaches), Coleoptera (beetles), Lepidoptera (butterflies and moths), Psocoptera (booklice), Acari (mites) and Hemiptera (bed bugs).	Gas application device.	100 %	Fumigant	CO_2 is used as a fumigant insecticide in a fumigation bubble built on purpose.	Not applicable, as product is not applied directly to crops or foodstuffs.	A minimum concentration of 60% v/v carbon dioxide must be achieved in a fumigation bubble.			None.

APPENDIX III: LIST OF STUDIES

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 "Yes" in the "Data Protection Claimed" column of the table below. Data protection is claimed under Article 12.1(c) (i) or (ii) and the claims can be found in Doc III-A and Doc III-B. 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 was however not possible to confirm the accuracy of this information.

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A2.1	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
A2.2	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
A2.4.1	European Chemicals Bureau	2003	Details for carbon dioxide ECB-EINECS Information System. http://ecb.jrc.it/new-chemicals/ / Published. Applicant's reference number CO2 239	No	PUB	Yes
A2.4.2	European Chemicals Bureau	2003	Details for carbon dioxide ECB-EINECS Information System. http://ecb.jrc.it/new-chemicals/ / Published. Applicant's reference number CO2 239	No	PUB	Yes
A2.5.1	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A2.5.2	Anon	2002	On-line calculation of Partition Coefficient for Carbon Dioxide http://esc.syrres.com/interkow/kowdemo.htm / Published Applicant's reference number CO2 114	No	PUB	Yes
A2.5.3	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
A2.6	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes
A2.9	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	No
A2.10/01	Rentokil Initial plc	2006	Manufacture of Carbon Dioxide : PT18 - Insecticide Unpublished Applicant's reference number CO2 243a	Yes	ORG	No
A2.10/02	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A2.10/03	Environmental Protection Agency	1981	Carbon dioxide, nitrogen, and combustion product gas; tolerances for pesticides in food administered by the Environmental Protection Agency. US Federal Register Vol 46, No 122, pp 32865-66 / Not GLP / Published Applicant's reference number CO2 291	No	PUB	No
A3.1.1/01	European Commission	1997	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 / Published	No	PUB	Yes
A3.1.1/02	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
A3.1.2/01	European Commission	1997	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 / Published	No	PUB	Yes
A3.1.2/02	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A3.1.3/01	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
A3.1.3/02	Anon	2003	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 / Published Applicant's reference number CO2 229	No	PUB	Yes
A3.2/01	Anon	2003	Raoult's Law and Phase Equilibria. www.jcsu.jesus.cam.ac.uk/~rpc25/notes/chemistry/phase_equilibria/ /Published Applicant's reference number CO2 228	No	PUB	Yes
A3.3.1	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
A3.3.2	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
A3.3.3	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A3.4.1	Thompson BA Harteck P Reeves RR Jnr.	1963	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 Not GLP / Published Applicant's reference number CO2 175	No	PUB	Yes
A3.4.2	Stein SE	2001	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 No data about GLP / Published Applicant's reference number CO2 178	No	PUB	Yes
A3.4.3/01	Stothers JB	1972	Carbon-13 NMR Spectroscopy. Academic Press Pages 279-310 Not GLP / Published. Applicant's reference number CO2 218	No	PUB	Yes
A3.4.3/02	Ettinger R Blume P Patterson A	1960	C13 Chemical Shifts in CO and CO2 The Journal of Chemical Physics Vol 33 No. 5 Pages 1597-1598 Not GLP / Published Applicant's reference number CO2 213	No	PUB	Yes
A3.4.4	Stein SE	2001	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 No data about GLP / Published Applicant's reference number CO2 179	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A3.5/01	Lide DR Frederikse HPR	1995	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 / Published. Applicant's reference number CO2 182	No	PUB	Yes
A3.5/02	Budavari S, O'Neil MJ, Smith A, Heckelman PE and Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
A3.6	United States Environmental Protection Agency	1996	EPA Product Properties Test Guidelines OPPTS 830.7370 Dissociation Constants in Water EPA 712-C-96-036 / Published	No	PUB	Yes
A3.7/01	Battino R Evans FD, Danforth WF Wilhelm E	1971	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 Not GLP / Published. Applicant's reference number CO2 220	No	PUB	Yes
A3.7/02	Battino R Evans FD Danforth WF	1968	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 Not GLP / Published. Applicant's reference number CO2 230	No	PUB	No
A3.7/03	Cauquil G	1927	Solubilitie de Quelques Gaz Dans le Cyclohexanol J Chem Phys Vol 24 pages 53-55 Not GLP / Published. Applicant's reference number CO2 222	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A3.7/04	Blanchard F Carre B Biensan P Lemordant D	2002	Study of the Carbon Dioxide Solubility in Solvent and Electrolytes used in Lithium Ion Batteries. www.univ-tours.fr/ed/edsst/comm2002/blanchard. pdf Not GLP / Published. Applicant's reference number CO2 255	No	PUB	No
A3.7/05	Chemical Sciences	2004	Henry's Law and the Solubility of Gases From: www.psigate.ac.uk/newsite/reference/plambeck/chem2/p01182.htm / Published. Applicant's reference number CO2 256	No	PUB	No
A3.9/01	Battino R Evans FD, Danforth WF Wilhelm E	1971	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 Not GLP / Published. Applicant's reference number CO2 220	No	PUB	Yes
A3.9/02	Anon	2002	On-line calculation of Partition Coefficient for Carbon Dioxide http://esc.syrres.com/interkow/kowdemo.htm / Published Applicant's reference number CO2 114	No	PUB	Yes
A3.9/03	Anon	2004	Octanol-Water Partition Coefficient Estimation by JAVA Applet http://www.pirika.com/chem/TCPEE/LOGKOW/ourlogkow.htm / Published. Applicant's reference number CO2 257	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A3.9/04	European Commission	2003	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 / Published.	No	PUB	Yes
A3.10/01	Greenwood NN Earnshaw A	1984	Chapter 8.6 Oxides and Carbonates. Chemistry of the Elements First Edition. Page 325-333 Pergamon Press plc. ISBN 0-08-022057-6 / Published Applicant's reference number CO2 190	No	PUB	Yes
A3.10/02	Lietzke MH Mullins C	1981	The Thermal Decomposition of Carbon Dioxide. J. Inorg. Nucl. Chem. Vol 43. pages 1769-1771 Not GLP / Published. Applicant's reference number CO2 207	No	PUB	Yes
A3.12	European Commission	1997	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 / Published	No	PUB	Yes
A3.13	European Commission	1997	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 / Published	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A3.15	European Commission	1997	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 / Published	No	PUB	Yes
A3.16	European Commission	1997	Method A.17 Oxidising 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 / Published	No	PUB	Yes
A3.17/01	British Standard	2000	Transportable Gas Cylinders - Specification for the design and construction of refillable transportable seamless steel gas cylinders of water capacities from 0,5 litre up to and including 150 litres - Part 1: Cylinders made of seamless steel with an Rm value of less than 1100MPa British Standard BS 1964-1:2000 Published. Applicant's reference number: CO2 299	No	PUB	No
A3.17/02	British Standard	1982	Transportable gas containers - Part 1: Specification for seamless steel gas containers above 0.5 litre water capacity. British Standard 5045-1:1982. Published Applicants reference number: CO2 300	No	PUB	No
A4.1	Messer UK Ltd	2004	Validation of Analytical Methods Used to Determine the Percentage Concentration of Carbon Dioxide, GLP / Unpublished. Applicant's reference number CO2 252a	Yes	ORG	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A4.3	Environmental Protection Agency	1981	Carbon dioxide, nitrogen, and combustion product gas; tolerances for pesticides in food administered by the Environmental Protection Agency. US Federal Register Vol 46, No 122, pp 32865-66 / Not GLP / Published Applicant's reference number CO2 291	No	PUB	No
A5.3/01	Rentokil Ltd	1990	Overview of Efficacy Data for Carbon Dioxide Used as a Fumigant (at 35 degrees centigrade and 60% in air). Not GLP. Unpublished. Applicants reference no. CO2 67	Yes	ORG	No
A5.3/02	Jay E G	1986	Factors affecting the use of carbon dioxide for treating raw and processed agricultural products. U.S. Department of Agriculture. Not GLP. Published. Applicants reference no. CO2 19	No	PUB	No
A5.3/03	Ministry of Agriculture, Fisheries and Food. Agricultural Science Service	1982	Research and development report. Storage Pests. Reference book 251 (82). HMSO. 33-34. Not GLP. Published. Applicants reference no. CO2 14.	No	PUB	No
A5.3/04	Banks H J	1978	Recent advances in the use of modified atmospheres for stored product pest control. In Proceedings of the 2nd International Working Conference on Stored Product Entomology, Ibadan. 198-217. CSIRO. Not GLP. Published. Applicants reference no. CO2 23	No	PUB	No
A5.3/05	Jay EG	1971	Suggested conditions and procedures for using carbon dioxide to control insects in grain storage facilities. US Agric. Res. Ser. (Rep) ARS 51-46. Not GLP. Published. 287	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A5.3/06	Navarro S	1978	The effects of low oxygen tensions on three stored-product insect pests. Phytoparasitica 6 (2): 51-58.Not GLP. Published. Applicants reference no. CO2 30	No	PUB	No
A5.3/07	Pearman G C & Jay E G	1970	The effect of relative humidity on the toxicity of carbon dioxide to Tribolium castaneum in peanuts. J. Georgia Entomol. Soc. 5 (2):61-64. Not GLP. Published. Applicants reference no. CO2 26	No	PUB	No
A5.3/08	Rentokil Ltd	1989	Efficacy against insects and mites of fumigation with atmospheres containing 60% carbon dioxide. Technical Committee Report No. PCS 89/30. Not GLP. Unpublished. Applicants reference no. CO2 21.	Yes	ORG	No
A5.3/09	Benschoter C A	1987	Effects of modified atmospheres and refrigeration temperatures on survival of eggs and larva of the Caribbean fruit fly (Diptera: Tephritidae) in laboratory diet. J. Econ. Entomol. 80 (6), 1223-1225. Not GLP. Published. Applicants reference no. CO2 286	No	PUB	No
A5.3/10	Oosthuizen M J & Schmidt U W	1942	The toxicity of carbon dioxide in the cowpea weevil. J. ent. Soc. S. Afr. 5, 99-110. Not GLP. Published. Applicants reference no. 282	No	PUB	No
A5.3/11	Rentokil Limited	1989	Susceptibility of insects and mites to fumigation with atmospheres containing 60, 80 and 100% carbon dioxide (225/2). Technical Committee Report No. PCS 89/4. Not GLP. Unpublished. Applicants reference no. CO2 22.	Yes	ORG	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A5.3/13	Childs D P & Overby J E	1983	Mortality of the cigarette beetle in high-carbon dioxide atmospheres. Journal of Economic Entomology 76 (3):544-546. Not GLP. Published. Applicants reference no. CO2 24.	No	PUB	No
A5.3/14	Keever D W	1989	Use of carbon dioxide to disinfest a tobacco warehouse of the cigarette beetle. J. Agric. Entomol. 6 (1): 43-51. Not GLP. Published. Applicants reference no. CO2 34.	No	PUB	No
A5.3/15	Navarro S & Jay E G	1987	Application of modified atmospheres for controlling stored grain insects. In Stored Products Pests Control. BPCS Symposium 229-236. Not GLP. Published. Applicants reference no. CO2 10.	No	PUB	No
A5.3/16	Harein P K & Press A F	1968	Mortality of stored-peanut insects exposed to mixtures of atmospheric gases at various temperatures. J. stored Prod. Res. 4:77-82. Not GLP. Published. Applicants reference no. CO2 35	No	PUB	No
A5.3/17	Marzke F O, Press A F & Pearman G C	1970	Mortality of the Rice weevil, the Indian Meal moth, and Trogoderma glabrum exposed to mixtures of atmospheric gases at various temperatures. Journal of Economic Entomology 63 (2): 570-574. Not GLP. Published. Applicants reference no. CO2 15	No	PUB	No
A5.3/18	Jay E G, Arbogast R T & Pearman G C	1971	Relative humidity: Its importance in the control of stored-product insects with modified atmospheric gas concentrations. J. stored Prod Res. 6:325-329. Not GLP. Published. Applicants reference no. CO2 13	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A5.3/19	Spratt E, Dignan G & Banks H J	1985	The effects of high concentrations of carbon dioxide in air on Trogoderma granarium Everts (Coleoptera: Dermestidae). J. stored Prod. Res 12 (1): 41-46. Not GLP. Published. Applicants reference no. CO2 12	No	PUB	No
A5.3/20	Aliniazee M T	1971	The effect of carbon dioxide gas alone or in combinations on the mortality of Tribolium castaneum (Herbst) and T. confusum du val (coleoptera, tenebrionidae). J. stored Prod. Res. 7:243-252. Not GLP. Published. Applicants reference no. CO2 41.	No	PUB	No
A5.3/21	Jay E	1984	Control of Rhyzoptera dominica with modified atmospheres at low pressure temperatures. J. Agric. Entomol. 1 (2): 155-160.Not GLP. Published. Applicants reference no. CO2 33.	No	PUB	No
A5.3/22	Navarro S & Calderon M	1974	Exposure to Ephestia cautella (WLK.) pupae to carbon dioxide concentrations at different relative humidities: the effect on adult emergence and loss in weight. J. stored Prod. Res. 10:237-241. Not GLP. Published. Applicants reference no. CO2 29	No	PUB	No
A5.3/23	Nicolas G & Sillans D	1989	Immediate and latent effects of carbon dioxide on insects. Annu. Rev. Entomol. 34:97-116. Not GLP. Published. Applicants reference no. CO2 74.	No	PUB	No
A5.3/24	Hashem M Y, Reichmuth C	1994	Interactive effects of high carbon dioxide or low-oxygen atmospheres and temperatures on hatchability of eggs of three stored-product insects. Zeitschrift fuer Pflanzenkrankheiten und Pflanzenschutz 101 (2): p 178-182. Not GLP. Published. Applicants reference no. CO2 313.	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A5.3/27	Insect R&D Limited	2005	Report of tests to evaluate the activity of 60% carbon dioxide (CO2) against adult bed bugs, *Cimex lectularius*. Report No: REN/CIM/CO2/06.05 Not GLP / Unpublished Applicants reference no. CO2 322	Yes	ORG	No
A5.3/28	Rentokil Initial UK Ltd	2006	Measurement of carbon dioxide levels in a bubble and efficacy against *Blatella germanica*. Not GLP / Unpublished Applicant's reference number CO2 323	Yes	ORG	No
A5.3/29	Krishnamurthy T S, Spratt E C, Bell C H	1986	The toxicity of carbon dioxide to adult beetles in low oxygen atmospheres. J, stored Prod. Res. 22 (3): 145-151. Not GLP / Published. Applicant's reference number CO2 326	No	PUB	No
A5.3/30	Thurig B, Korner C, Stocklin J	2003	Seed production and seed quality in a calcareous grassland in elevated CO2. Global Change Biology 9, 873-884 Not GLP / Published. Applicant's reference number CO2 327	No	PUB	No
A5.3/31	Rentokil Initial UK Ltd	2006	Efficacy of Carbon Dioxide against *Sitophilus granarius* (adults) in Fumigation Bubbles. Project No. 225/07 Report No. SS06/05 Not GLP / Unpublished. Applicant's reference number CO2 328	Yes	ORG	No
A5.4.1/01	Nicolas G, Sillans D. 1989		Immediate and latent effects of carbon dioxide on insects. Ann. Rev. Entomol. 1989 34:97-116 Not GLP. Published. Applicants reference no. CO2 74	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A5.4.1/02	Anon	2003	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 / Published. Applicant's reference number: CO2 237	No	PUB	No
A5.7.1	Anon	2003	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 / Published. Applicant's reference number CO2 238	No	PUB	No
A6.1.3/01	Sechzer PH Egbert LD Linde HW Cooper DY Dripps RD Price HL	1960	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 Not GLP / Published. Applicant's reference number CO2 131	No	PUB	Yes
A6.1.3/02	Barbour JH Seevers MH	1942	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 Not GLP / Published. Applicant's reference number CO2 81	No	PUB	Yes
A6.1.3/03	US Army Medical Research	1994	Live Fire Support Services Expansion of the N Gas Model for Toxic Potency to Include NO2 Effects. Jaycor 2904-01 Not GLP / Published. Applicant's reference number CO2 98	No	PUB	Yes

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A6.1.3/04	Morita M Tabata N	1988	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 Not GLP / Published. Applicant's reference number CO2 97	No	PUB	Yes
A6.1.3/05	Brown EB Jr. Miller F	1952	Ventricular Fibrillation Following a Rapid Fall in Alveolar Carbon Dioxide Concentration Am. J. Physiol Vol 169 pages 56-60 Not GLP / Published. Applicant's reference number CO2 118	No	PUB	Yes
A6.1.3/06	Luft US Finklestein S Elliot JC	1974	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 Not GLP / Published. Applicant's reference number CO2 155	No	PUB	Yes
A6.1.3/07	Cullen DJ Eger E I	1974	Cardiovascular Effects of Carbon Dioxide in Man Anesthesiology Vol 41, pages 345-349 Not GLP / Published. Applicant's reference number CO2 132	No	PUB	Yes
A6.1.3/08	Blackburn JP Conway CM Leigh LM Lindop MJ Reitan JA	1972	PaCo2 and the Pre-ejection Period: The PaCo2/Inotrophy Response Curve Anesthesiology Vol 37, No 3 pages 268-276 Not GLP / Published. Applicant's reference number CO2 133	No	PUB	Yes

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A6.1.3/09	Nahas GG Steinsland OS	1968	Increased Rate of Catecholeamine Synthesis During Respiratory Acidosis Respiration Physiology Vol 5, pages 108-117 Not GLP / Published. Applicant's reference number CO2 176	No	PUB	Yes
A6.1.3/10	Alexander W Duff P Haldane JBS Ives G Renton D	1939	After Effects of Exposure of Men to Carbon Dioxide Lancet Vol 2, pages 419-420 Not GLP / Published. Applicant's reference number CO2 195	No	PUB	Yes
A6.1.3/11	Poyart C Nahas GG	1966	Inhibition of Catecholamine-Induced Calorigenesis and Lipolysis by Hypercapnic Acidosis Am J Physiol Vol 211 pages 161-168 Not GLP / Published Applicant's reference number CO2 201	No	PUB	Yes
A6.1.3/12	Richards JB Stein SN	1957	Effect of CO2 Exposure and Respiratory Acidosis on Adrenal 17-Hydroxycorticosteroid Secretion in Anesthetized Dogs Am J Physiol Vol 188 pages 1-6 Not GLP / Published. Applicant's reference number CO2 206	No	PUB	Yes
A6.1.3/13	Krehl L Straub W	1928	Moderne Gewerbliche Vergiftungen. Naunyn-Schmiedebergs "Archiv fur Experimentelle Pathologie und Pharmakologie" pages 65-83 Verlag Von F.C.W in Leipzig Not GLP / Published Applicant's reference number CO2 83	No	PUB	Yes
A6.1.3/14	Morita M, Tabata N, Maya A	1985	Studies on Asphyxia : on the Changes of the Alveolar Walls of Rats in the Hypoxic State Forensic Science International 27 Pages 81-92 Not GLP / Published. Applicant's reference number CO2 135	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A6.2/01	Kinney JM	1960	Transport of Carbon Dioxide in Blood Anethesiology Vol 21, Number 6 pages 615-619 Not GLP / Published. Applicant's reference number CO2 150	No	PUB	Yes
A6.4.3/01	Anon	2002	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 / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.4.3/02	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
A6.4.3/03	Environmental Protection Agency	1991	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs / Published. Applicant's reference number CO2 91	No	PUB	Yes
A6.4.3/04	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
A6.4.3/05	McDowall RJS	1964	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 / Published. Applicant's reference number CO2 240	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A6.4.3/06	Tharr D	1988	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 Not GLP / Published. Applicant's reference number CO2 273	No	PUB	Yes
A6.4.3/07	Maiti H, Cheyne MF, Hobbs G Jeraj HA	1999	Cryotherapy Gas - to Use Nitrogen Oxide or Carbon Dioxide? Int J Std AIDS 1999, Feb 10 (2) 118-120 Not GLP / Published. Applicant's reference number CO2 274	No	PUB	Yes
A6.4.3/08	Faucett RE Newman PP	1953	Operation Hideout Preliminary Report: Report No. 228 US Naval Research Laboratory New London Conn / Not GLP / Published. Applicant's reference number: CO2 140	No	PUB	Yes
A6.4.3/09	Consolazio WV Fisher MB Pace N Pecora LJ Pitts GC Behnke AR	1947	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 Not GLP/ Published. Applicant's reference number CO2 198	No	PUB	Yes
A6.4.3/10	Brackett NC Wingo CF Muren O Solano JT	1969	Acid Base Response to Chronic Hypercapnia in Man The New England Journal of Medicine Pages 124-130 Not GLP / Published. Applicant's reference number CO2 200	No	PUB	Yes
A6.4.3/11	Stein SN Lee RE Annegers JH Kaplan SA McQuarrie DG	1959	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. / Not GLP / Published. Applicant's reference number: CO2 142	No	PUB	Yes

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A6.4.3/12	Barbour JH Seevers MH	1942	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 Not GLP / Published. Applicant's reference number CO2 81	No	PUB	Yes
A6.4.3/13	Barbour JH Seevers MH	1942	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 Not GLP / Published. Applicant's reference number CO2 81	No	PUB	Yes
A6.4.3/14	Schaefer KE McCabe N Withers J	1968	Stress Response in Chronic Hypercapnia American Journal of Physiology Vol. 214, No 3 Pages 543-548 Not GLP / Published. Applicant's reference number CO2 109	No	PUB	Yes
A6.4.3/15	Silber RH, Busch RD and Oslapas R	1958	Practical procedure for estimation of corticosterone or hydrocortisone. Clin Chem 4 278-285. Not GLP / Published. Applicant's reference number CO2 294	No	PUB	No
A6.4.3/16	Anton AH and Sayre DF	1962	A study of the factors affecting the aluminium oxide trihydroxyindole procedure for the analysis of catecholamines. J Pharmacol Exptl Therap 138: 360-375. Not GLP / Published. Applicant's reference number CO2 295	No	PUB	No
A6.4.3/17	Dole VP	1956	A relation between non-esterified fatty acids in plasma and the metabolism of glucose. J Clin. Invest 35: 150-154. Not GLP / Published. Applicant's reference number CO2 296	No	PUB	No

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A6.4.3/18	Trout DL, Ester Jr. EH, and Freidberg SJ	1960	Titration of free fatty acids of plasma: a study of current methods and a new modification.J Lipid Res. 1 199-202 Not GLP / Published. Applicant's reference number CO2 297	No	PUB	No
A6.4.3/19	Kingsley GR and Schaffert RR	1949	Determination of free and total cholesterol by chloroform extraction. J Biol. Chem 180: 315-328. Not GLP / Published. Applicant's reference number CO2 298	No	PUB	No
A6.4.3/20	King CTG Williams EE Mego JL Schaefer KE	1955	Adrenal Function During Prolonged Exposure to Low Concentration of Carbon Dioxide Am J Physiol Vol 180, Pages 46-52 Not GLP / Published. Applicant's reference number CO2 210	No	PUB	Yes
A6.4.3/21	Randolph T G	1944	Blood studies in allergy. I - The direct counting chamber determination of eosinophils by propylene glycol aqueous stains. J. Allergy 15 : 89-96. Not GLP / Published. Applicant's reference number CO2 301	No	PUB	No
A6.4.3/22	Van Slyke D D and Sendroy J	1928	Studies of gas and electrolyte equilibria in blood. XV. Line charts for graphic calculations by the Henderson-Hasselbach equation, and for calculating plasma carbon dioxide contrent from whole blood content. J. Biol. Chem. 79: 781-798 Not GLP / Published. Applicant's reference number CO2 302	No	PUB	No
A6.4.3/23	Good C A, Kramer H and Somogyi M	1933	The determination of glycogen. J. Biol. Chem. 100: 485-491 Not GLP / Published. Applicant's reference number CO2 303	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A6.4.3/24	Roe J H and Kuether C A	1943	The determination of ascorbic acid in whole blood and urine through the 2,4-dinitrophenylhydrazine derivative of dehydroascorbic acid. J. Biol. Chem. 147: 399-407 Not GLP / Published. Applicant's reference number CO2 304	No	PUB	No
A6.4.3/25	Kingsley GR and Schaffert RR	1949	Determination of free and total cholesterol by chloroform extraction. J Biol. Chem 180: 315-328. Not GLP / Published. Applicant's reference number CO2 298	No	PUB	No
A6.4.3/26	Dixon W J and Mood A M	1946	The statistical sign test. J. Am. Statistical Ass. 41: 557-566 Not GLP / Published. Applicant's reference number CO2 305	No	PUB	No
A6.4.3/27	Bloch K	1945	The biological conversion of cholesterol to pregnanediol. J. Biol. Chem. 157: 661-666. Not GLP / Published. Applicant's reference number CO2 306	No	PUB	No
A6.4.3/28	Claesson L and Hillarp N-A	1947	Critical remarks on the histochemical reactions for ketosteroids. Acta. Anal. 3: 109-114 Not GLP / Published. Applicant's reference number CO2 307	No	PUB	No
A6.4.3/29	Levin L	1945	The effects of several varieties of stress on the cholesterol content of the adrenal glands and of the serum of rats. Endocrinology 37: 34-43 Not GLP / Published. Applicant's reference number CO2 308	No	PUB	No
A6.4.3/30	Rentokil Initial plc	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished. Applicant's reference number CO2 321	Yes	ORG	No

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A6.4.3/31	Rentokil Initial plc	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished. Applicant's reference number CO2 329	Yes	ORG	No
A6.5/01	Nahas G	1974	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. Not GLP / Published. Applicant's reference number CO2 136	No	PUB	Yes
A6.5/02	McDowall RJS	1964	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 Not GLP / Published. Applicant's reference number CO2 240	No	PUB	Yes
A6.5/03	Schaefer KE McCabe N Withers J	1968	Stress Response in Chronic Hypercapnia American Journal of Physiology Vol. 214, No 3 Pages 543-548 Not GLP / Published. Applicant's reference number CO2 109	No	PUB	Yes
A6.5/04	Schaefer KE	1961	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 401-413 Not GLP / Published. Applicant's reference number CO2 108	No	PUB	Yes
A6.5/05	Environmental Protection Agency	1991	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs / Published. Applicant's reference number CO2 91	No	PUB	Yes

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A6.5/06	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes
A6.5/07	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
A6.5/08	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
A6.5/09	Anon	2003	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 / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.6.1/01	Anon	2003	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 / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.6.1/02	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes

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A6.6.1/03	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
A6.6.1/04	Environmental Protection Agency	1991	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs / Published. Applicant's reference number CO2 91	No	PUB	Yes
A6.6.1/05	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes
A6.6.2/01	Anon	2003	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 / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.6.2/02	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
A6.6.2/03	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No

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A6.6.2/05	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes
A6.6.3/01	Anon	2003	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 / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.6.3/02	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
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A6.6.3/05	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes
A6.6.4/01	Anon	2003	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 / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.6.4/02	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
A6.6.4/03	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
A6.6.4/04	Environmental Protection Agency	1991	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs / Published. Applicant's reference number CO2 91	No	PUB	Yes
A6.6.4/05	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes

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A6.7/01	Nahas G	1974	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. Not GLP / Published. Applicant's reference number CO2 136	No	PUB	Yes
A6.7/02	McDowall RJS	1964	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 / Published. Applicant's reference number CO2 240	No	PUB	Yes
A6.7/03	Schaefer KE McCabe N Withers J	1968	Stress Response in Chronic Hypercapnia American Journal of Physiology Vol. 214, No 3 Pages 543-548 Not GLP / Published. Applicant's reference number CO2 109	No	PUB	Yes
A6.7/04	Schaefer KE	1961	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 401-413 Not GLP / Published. Applicant's reference number CO2 108	No	PUB	Yes
A6.7/05	Environmental Protection Agency	1991	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs / Published. Applicant's reference number CO2 91	No	PUB	Yes

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A6.7/06	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes
A6.7/07	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
A6.7/08	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
A6.7/09	Anon	2003	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 / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.8.1/01	Anon	2003	Environmental Management Indicators and Environmental Accounting Basic Thinking for Environmental Management Indicators and Environmental Accounting http://www.kirinco.jp/english/company/env/p12_13.html / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.8.1/02	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes

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A6.8.1/03	Environmental Protection Agency	1991	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs / Published. Applicant's reference number CO2 91	No	PUB	Yes
A6.8.1/04	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
A6.8.1/05	Haring OM	1960	Cardiac Malformations in Rats Induced by Exposure of the Mother to Carbon Dioxide During Pregnancy Circulation Research, Vol VIII, pages 1218-1223 Not GLP/ Published. Applicant's reference number CO2 107	NO	PUB	Yes
A6.8.1/06	Vandemark NL Schanbacher BD Gomes WR	1972	Alterations in Testes of Rats Exposed to Elevated Atmospheric Carbon Dioxide J Reprod. Fert Vol 28, pages 457-459 Not GLP / Published. Applicant's reference number CO2 111	No	PUB	Yes
A6.8.1/07	Mukherjee DP Singh SP	1967	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 Not GLP / Published. Applicant's reference number CO2 110	No	PUB	Yes
A6.8.1/08	Grote W	1965	Interference with Embryo Development with Increased CO2 and O2 Partial Pressure and with Under-Pressure Z Morpholol Anthropol vol 56, pp 165-194 Not GLP / Published Applicant's reference number CO2 280	No	PUB	Yes

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A6.8.2/01	Nahas G	1974	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. Not GLP / Published. Applicant's reference number CO2 136	No	PUB	Yes
A6.8.2/02	McDowall RJS	1964	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 / Published. Applicant's reference number CO2 240	No	PUB	Yes
A6.8.2/03	Schaefer KE McCabe N Withers J	1968	Stress Response in Chronic Hypercapnia American Journal of Physiology Vol. 214, No 3 Pages 543-548 Not GLP / Published. Applicant's reference number CO2 109	No	PUB	Yes
A6.8.2/04	Schaefer KE	1961	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 Not GLP / Published. Applicant's reference number CO2 108	No	PUB	Yes
A6.8.2/05	Environmental Protection Agency	1991	Re-registration Eligibility Document (RED) Carbon and Carbon Dioxide United States Environmental Protection Agency, Office of Pesticide Programs / Published. Applicant's reference number CO2 91	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A6.8.2/06	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient US Department of Commerce, National Technical Information Service / Published Applicant's reference number CO2 96	No	PUB	Yes
A6.8.2/07	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
A6.8.2/08	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
A6.8.2/09	Anon	2003	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 / Published. Applicant's reference number CO2 137	No	PUB	Yes
A6.9/01	Messer UK Ltd	2000	Safety Data Sheet for Carbon Dioxide (Refrigerated Liquid) dated 10/02/2000 Version 03	No	PUB	Yes
A6.9/02	Alexander W, Duff P, Haldane JBS, Ives G, Renton D	1939	After Effects of Exposure of Men to Carbon Dioxide Lancet Vol 2, pages 419-420 Not GLP/ Published Applicant's reference number CO2 195	No	PUB	Yes
A6.9/03	Consolazio WV Fisher MB Pace N Pecora LJ Pitts GC Behnke AR	1947	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 Not GLP/ Published Applicant's reference number CO2 198	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A6.9/04	Sechzer PH Egbert LD Linde HW Cooper DY Dripps RD Price HL	1960	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 Not GLP/ Published Applicant's reference number CO2 131	No	PUB	Yes
A6.9/05	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
A6.12/01	Riley RL Barnea-Bromberger B	1979	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 Not GLP / Published. Applicant's reference number CO2 205	No	PUB	Yes
A6.12/02	Luft US, Finklestein S Elliot JC	1974	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 Not GLP/ Published Applicant's reference number CO2 155	No	PUB	Yes
A6.12/03	Schaefer KE	1961	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 401-413 Not GLP/ Published Applicant's reference number CO2 108	No	PUB	Yes
A6.12/04	Messer UK Ltd	2000	Safety Data Sheet for Carbon Dioxide (Refrigerated Liquid) dated 10/02/2000 Version 03	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A6.12/05	Alexander W, Duff P, Haldane JBS, Ives G, Renton D	1939	After Effects of Exposure of Men to Carbon Dioxide Lancet Vol 2, pages 419-420 Not GLP/ Published Applicant's reference number CO2 195	No	PUB	Yes
A6.12/06	Consolazio WV Fisher MB Pace N Pecora LJ Pitts GC Behnke AR	1947	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 Not GLP/ Published Applicant's reference number CO2 198	No	PUB	Yes
A6.12/07	Sechzer PH Egbert LD Linde HW Cooper DY Dripps RD Price HL	1960	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 Not GLP/ Published Applicant's reference number CO2 131	No	PUB	Yes
A6.12.5	Rentokil Initial UK Ltd	2007	Safety Data Sheet for Carbon Dioxide Issue 04 / Published.	No	PUB	No
A6.12.7	Rentokil Initial UK Ltd	2007	Safety Data Sheet for Carbon Dioxide Issue 04 / Published.	No	PUB	No
A6.12.8/01	Rentokil Initial UK Ltd	2007	Safety Data Sheet for Carbon Dioxide Issue 04 / Published.	No	PUB	No
A6.12.8/02	Goodman LS Gilman A	1980	Goodman and Gilmans The Pharmacological Basis of Therapeutics. Sixth Edition Pages 331-334 ISBN 0-02-344720-6 / Published. Applicant's reference number CO2 82	No	PUB	Yes
A6.15/01	Commodity Storage Group Ltd	1989	Carbon dioxide in food treatment. Published / Applicants reference CO2 18	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A6.15/02	Environmental Protection Agency	1981	Carbon dioxide, nitrogen, and combustion product gas; tolerances for pesticides in food adminsitered by the Environmental Protection Agency. US Federal Register Vol 46, No 122, pp 32865-66, June 25 1981. Published / Applicants reference CO2 291.	No	PUB	No
A6.15/03	Jukes D	2002	Food Additives in the European Union http://www.fst.rdg.ac.uk/foodlaw/ additive.htm Published / Applicants reference CO2 124	No	PUB	No
A7.1.1.1.1/01	Anon	2005	The Carbon Cycle. From: www.physicalgeography.net/fundamentals/9r.html Not GLP/ Published Applicant's reference number CO2 268	No	PUB	No
A7.1.1.1.1/02	Anon	2005	Carbon Cycle. From: www.lenntech.com/carbon-cycle.htm Not GLP/ Published Applicant's reference number CO2 269	No	PUB	No
A7.1.1.1.1/03	Anon	2005	Cellular Respiration. From: http://en.wikipedia.org/wiki/Cellular_respiration Not GLP/ Published Applicant's reference number CO2 270	No	PUB	No
A7.1.1.1/04	Anon	2005	Weathering. From: http://regentsprep.org/Regents/earthsci/units/weathering/weathering.cfm Not GLP/ Published Applicant's reference number CO2 271	No	PUB	No
A7.1.1.1/05	Anon	2005	The Carbon Cycle and Earth's Climate. From: www.columbia.edu/~vjd1/carbon.htm Not GLP/ Published Applicant's reference number CO2	No	PUB	No

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A7.1.1.1.2	Thompson BA Harteck P Reeves RR Jr	1963	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 Not GLP / Published Applicant's reference number CO2 175	No	PUB	Yes
A7.1.1.2.1	Jones J, Mulholland PJ	1988	Influence of Drainage Basin Topography and Elevation on Carbon Dioxide and Methane Supersaturation of Stream Water Biogeochemistry 40: 57-72, Not GLP / Published Applicant's reference number CO2 275	No	PUB	Yes
A7.2.1	Hamada Y Tanaka T	2001	Dynamics of Carbon Dioxide in Soil Profiles Based on Long-Term Field Observation Hydrological Processes 15, 1829-1845 Not GLP / Published. Applicant's reference number CO2 279.	No	PUB	Yes
A7.4.1.1/01	Ross R M Krise W F Redell L A Bennett RM	2001	Effects of Dissolved Carbon Dioxide on the Physiology and Behaviour of Fish in Artifical Streams Environmental Toxicology Vol 16 pages 84-95 Not GLP / Published Applicant's reference number CO2 129	No	PUB	Yes
A7.4.1.1/02	Alabaster JS Herbert DWM Hemens J	1957	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 Not GLP / Published Applicant's reference number CO2 125	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A7.4.1.2/01	Paul RJ, Colmorgen M, Pirow R, Chen YH, Tsai MC	1988	Systemic and Metabolic Responses in Daphnia magna to anoxia Comparative Biochemistry and Physiology Part A 120, 519-530 Not GLP / Published. Applicant's reference number CO2 278	No	PUB	Yes
A7.4.1.2/02	Battish SK Kumari P	1986	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 Not GLP / Published. Applicant's reference number CO2 276	No	PUB	Yes
A7.4.1.2/03	Nielsen MG, Christian K, Birkmose D	2003	Carbon dioxide concentrations in the nests of the mud dwelling mangrove ant Polyrhachis sokolova Forel (Hymenoptera: Formicidae) Australian Journal of Entomology 42, 357-362 Not GLP / Published. Applicant's reference number CO2 277	No	PUB	Yes
A7.4.1.4	Todar K	2002	Physical and Environmental Requirements for Microbial Growth www.bact.wisc.edu/MicrotextBook/NutritionGrowth/physicalandenv.html / Published. Applicant's reference number CO2 95	No	PUB	Yes
A7.5.1.2	Zaller JG Arnone III, JA	1997	Activity of surface-casting earthworms in a calcareous grassland under elevated atmospheric CO2. Oecologica Vol 111 pages 249-254 Not GLP / Published Applicant's reference number CO2 212	No	PUB	Yes

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner PUB/ORG	Already submitted for PT14 (Yes/No)
A7.5.3.1.1/01	Huffman H	2003	Minimum Ventilation www.gov.on.ca/OMAFRA/english/livestock/poultry/facts/min_vent.htm / Published Applicant's reference number CO2 215	No	PUB	Yes
A7.5.3.1.1/02	UK Home Office	1986	The Humane Killing of Animals under Schedule 1 to the Animals (Scientific Procedures) Act 1986 Code of Practice The Stationery Office Limited / Published Applicant's reference number: CO2 139	No	PUB	Yes
A7.5.5	Anon	2003	Fundamentals of Physical Geography. Introduction to Biogeography and Ecology The Carbon Cycle. www.geog.ouc.bc.ca/physgeog/contents/9r.html / Published Applicant's reference number CO2 216	No	PUB	Yes
A7.5.5.1	Anon	2003	Fundamentals of Physical Geography. Introduction to Biogeography and Ecology The Carbon Cycle. www.geog.ouc.bc.ca/physgeog/contents/9r.html / Published Applicant's reference number CO2 216	No	PUB	Yes
A8.1/01	Rentokil Initial UK Ltd	2007	Safety Data Sheet for Carbon Dioxide Issue 04 / Published.	No	PUB	No
A8.1/02	Messer UK Ltd	1997	Properties of Carbon Dioxide Leaflet No. 22000369 / Published Applicant's reference number CO2 75	No	PUB	No
A8.2	Rentokil Initial UK Ltd	2007	Safety Data Sheet for Carbon Dioxide Issue 04 / Published.	No	PUB	No
A8.3	Rentokil Initial UK Ltd	2007	Safety Data Sheet for Carbon Dioxide Issue 04 / Published.	No	PUB	No
A8.4	Rentokil Initial UK Ltd	2004	Safety Data Sheet for Carbon Dioxide dated 01/07/2004 Issue 02 / Published.	No	PUB	No

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B2.2/01	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
B2.2/02	European Chemicals Bureau	2003	Details for carbon dioxide ECB-EINECS Information System. http://ecb.jrc.it/new-chemicals/ / Published. Applicant's reference number CO2 239	No	PUB	No
B2.3.1	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
B2.3.2	Budavari S, O'Neil MJ, Smith A, Heckelman PE Kinneary JF	1996	Entry for Carbon Dioxide, The Merck Index An Encyclopedia of Chemicals, Drugs and Biologicals. Twelfth Edition Page 295 Merck Research Laboratories, ISBN 0911910-12-3 / Published	No	PUB	Yes
B5.1.2/01	Rentokil Initial UK Ltd	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished Applicant's reference number CO2 321	Yes	ORG	No
B5.1.2/02	Rentokil Initial UK Ltd	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished Applicant's reference number CO2 321	Yes	ORG	No
B5.1.2/03	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
B5.1.2/04	Rentokil Initial UK Ltd	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished	Yes	ORG	No

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			Applicant's reference number CO2 329			
B5.1.2/05	Rentokil Initial UK Ltd	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished Applicant's reference number CO2 329	Yes	ORG	No
B5.2/01	Power Plastics	2006	Technical Specification for PVC coated polyester fabric. Unpublished. Applicant's reference number: CO2 319	Yes	ORG	No
B5.2/02	Power Plastics	2006	Technical Data Sheet for Fumaplas M12 Unpublished. Applicant's reference number: CO2 320	Yes	ORG	No
B5.7/01	Pratt S J, Rainer Reuss	2004	Scrubbing carbon dioxide prevents overestimation of insect mortality in log-duration static phosphine toxicity assays. Not GLP. Published. Applicants reference no. CO2 283	No	PUB	No
B5.7/02	Nicolas G & Sillans D	1989	Immediate and latent effects of carbon dioxide on insects. Annu. Rev. Entomol. 34:97-116. Not GLP. Published. Applicants reference no. CO2 74	No	PUB	No
B5.10.2/01	Rentokil Ltd	1990	Overview of Efficacy Data for Carbon Dioxide Used as a Fumigant (at 35 degrees centigrade and 60% in air). Not GLP. Unpublished. Applicants reference no. CO2 67	Yes	ORG	No
B5.10.2/02	Jay E G	1986	Factors affecting the use of carbon dioxide for treating raw and processed agricultural products. U.S. Department of Agriculture. Not GLP. Published. Applicants reference no. CO2 19.	No	PUB	No
B5.10.2/03	Ministry of Agriculture, Fisheries and Food. Agricultural Science Service	1982	Research and development report. Storage Pests. Reference book 251 (82). HMSO. 33-34. Not GLP. Published. Applicants reference no. CO2 14.	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner	Already submitted for PT14
B5.10.2/04	Banks H J	1978	Recent advances in the use of modified atmospheres for stored product pest control. In Proceedings of the 2nd International Working Conference on Stored Product Entomology, Ibadan. 198-217. CSIRO. Not GLP. Published. Applicants reference no. CO2 23	No	PUB	No
B5.10.2/05	Jay E G	1971	Suggested conditions and procedures for using carbon dioxide to control insects in grain storage facilities. US Agric. Res. Ser. (Rep) ARS 51-46. Not GLP. Published. Applicants reference no. 287	No	PUB	No
B5.10.2/06	Navarro S	1978	The effects of low oxygen tensions on three stored-product insect pests. Phytoparasitica 6 (2): 51-58.Not GLP. Published. Applicants reference no. CO2 30	No	PUB	No
B5.10.2/07	Pearman G C & Jay E G	1970	The effect of relative humidity on the toxicity of carbon dioxide to Tribolium castaneum in peanuts. J. Georgia Entomol. Soc. 5 (2):61-64. Not GLP. Published. Applicants reference no. CO2 26	No	PUB	No
B5.10.2/08	Rentokil Ltd	1989	Efficacy against insects and mites of fumigation with atmospheres containing 60% carbon dioxide. Technical Committee Report No. PCS 89/30. Not GLP. Unpublished. Applicants reference no. CO2 21.	Yes	ORG	No
B5.10.2/09	Benschoter C A	1987	Effects of modified atmospheres and refrigeration temperatures on survival of eggs and larva of the Caribbean fruit fly (Diptera: Tephritidae) in laboratory diet. J. Econ. Entomol. 80 (6), 1223-1225. Not GLP. Published. Applicants reference no. CO2 286	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner	Already submitted for PT14
B5.10.2/10	Oosthuizen M J & Schmidt U W	1942	The toxicity of carbon dioxide in the cowpea weevil. J. ent. Soc. S. Afr. 5, 99-110. Not GLP. Published. Applicants reference no. 282	No	PUB	No
B5.10.2/11	Rentokil Limited	1989	Susceptibility of insects and mites to fumigation with atmospheres containing 60, 80 and 100% carbon dioxide (225/2). Technical Committee Report No. PCS 89/4. Not GLP. Unpublished. Applicants reference no. CO2 22.	Yes	ORG	No
B5.10.2/13	Childs D P & Overby J E	1983	Mortality of the cigarette beetle in high-carbon dioxide atmospheres. Journal of Economic Entomology 6 (3):544-546. Not GLP. Published. Applicants reference no. CO2 24.	No	PUB	No
B5.10.2/14	Keever D W	1989	Use of carbon dioxide to disinfest a tobacco warehouse of the cigarette beetle. J. Agric. Entomol. 6 (1): 43-51. Not GLP. Published. Applicants reference no. CO2 34.	No	PUB	No
B5.10.2/15	Navarro S & Jay E G	1987	Application of modified atmospheres for controlling stored grain insects. In Stored Products Pests Control. BPCS Symposium 229-236. Not GLP. Published. Applicants reference no. CO2 10.	No	PUB	No
B5.10.2/16	Harein P K & Press A F	1968	Mortality of stored-peanut insects exposed to mixtures of atmospheric gases at various temperatures. J. stored Prod. Res. 4:77-82. Not GLP. Published. Applicants reference no. CO2 35	No	PUB	No
B5.10.2/17	Marzke F O, Press A F & Pearman G C	1970	Mortality of the Rice weevil, the Indian Meal moth, and Trogoderma glabrum exposed to mixtures of atmospheric gases at various temperatures. Journal of Economic Entomology 63 (2): 570-574. Not GLP. Published. Applicants	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner	Already submitted for PT14
			reference no. CO2 15			
B5.10.2/18	Jay E G, Arbogast R T & Pearman G C	1971	Relative humidity: Its importance in the control of stored-product insects with modified atmospheric gas concentrations. J. stored Prod Res. 6:325-329. Not GLP. Published. Applicants reference no. CO2 13	No	PUB	No
B5.10.2/19	Spratt E, Dignan G & Banks H J	1985	The effects of high concentrations of carbon dioxide in air on Trogoderma granarium Everts (Coleoptera: Dermestidae). J. stored Prod. Res 12 (1): 41-46. Not GLP. Published. Applicants reference no. CO2 12	No	PUB	No
B5.10.2/20	Aliniazee M T	1971	The effect of carbon dioxide gas alone or in combinations on the mortality of Tribolium castaneum (Herbst) and T. confusum du val (coleoptera, tenebrionidae). J. stored Prod. Res. 7:243-252. Not GLP. Published. Applicants reference no. CO2 41.	No	PUB	No
B5.10.2/21	Jay E	1984	Control of Rhyzoptera dominica with modified atmospheres at low temperatures. J. Agric. Entomol. 1 (2): 155-160.Not GLP. Published. Applicants reference no. CO2 33.	No	PUB	No
B5.10.2/22	Navarro S & Calderon M	1974	Exposure to Ephestia cautella (WLK.) pupae to carbon dioxide concentrations at different relative humidities: the effect on adult emergence and loss in weight. J. stored Prod. Res. 10:237-241. Not GLP. Published. Applicants reference no. CO2 29	No	PUB	No
B5.10.2/23	Hashem M Y, Reichmuth C	1994	Interactive effects of high carbon dioxide or low-oxygen atmospheres and temperatures on hatchability of eggs of three stored-product insects. Zeitschrift fuer Pflanzenkrankheiten und Pflanzenschutz 101 (2): p 178-182.	No	PUB	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner	Already submitted for PT14
			Not GLP. Published. Applicants reference no. CO2 313.			
B5.10.2/26	Insect R&D Limited	2005	Report of tests to evaluate the activity of 60% carbon dioxide (CO2) against adult bed bugs, *Cimex lectularius*. Report No: REN/CIM/CO2/06.05 Not GLP / Unpublished Applicant's reference number CO2 322	Yes	ORG	No
B5.10.2/27	Rentokil Initial plc	2006	Measurement of carbon dioxide levels in a bubble and efficacy against *Blatella germanica*. Not GLP / Unpublished Applicant's reference number CO2 323	Yes	ORG	No
B5.10.2/28	Krishnamurthy T S, Spratt E C, Bell C H	1986	The toxicity of carbon dioxide to adult beetles in low oxygen atmospheres. J, stored Prod. Res. 22 (3): 145-151. Not GLP / Unpublished. Applicant's reference number CO2 326	No	PUB	No
B5.10.2/29	Rentokil Initial UK Ltd	2006	Efficacy of Carbon Dioxide against *Sitophilus granarius* (adults) in Fumigation Bubbles. Project No. 225/07 Report No. SS06/05 Not GLP / Unpublished. Applicant's reference number CO2 328	Yes	ORG	No
B6.6/01	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient. US Department of Commerce, National Technical Information Service / Published. Applicant's reference number: CO2 96	No	PUB	Yes
B6.6/02	Rentokil Initial UK Ltd	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished Applicant's reference number CO2 321	Yes	ORG	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner	Already submitted for PT14
B6.6/03	Health and Safety Executive	2005	EH40/2005 Workplace Exposure Limits 2005 HSE Books ISBN 0-7176-2977-5 / Published	No	PUB	No
B6.6/04	Rentokil Initial UK Ltd	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished Applicant's reference number CO2 329	Yes	ORG	No
B6.6/05	Rentokil Pest Control	2003	Fumigation Risk Assessment and Checklists. Not GLP / Unpublished Applicant's reference number: CO2 331.	Yes	ORG	No
B6.6/06	Rentokil Initial UK Ltd	2007	Safety Data Sheet for Carbon Dioxide Issue 02 / Published.	No	PUB	No
B6.6/07	Rentokil Initial plc	2006	Pest Control Fumigation Manual Not GLP / Unpublished	Yes	ORG	No
B6.7.1.1	Environmental Protection Agency	1981	Carbon dioxide, nitrogen, and combustion product gas; tolerances for pesticides in food adminsitered by the Environmental Protection Agency. US Federal Register Vol 46, No 122, pp 32865-66 / Not GLP / Published Applicant's reference number CO2 291	No	PUB	No
B7.1/01	Federation of American Societies for Experimental Biology	1979	Evaluation of the Health Aspects of Carbon Dioxide as a Food Ingredient. US Department of Commerce, National Technical Information Service / Published. Applicant's reference number: CO2 96	No	PUB	Yes
B7.1/02	Rentokil Initial UK Ltd	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished Applicant's reference number CO2 321	Yes	ORG	No

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner	Already submitted for PT14
B7.1/03	Rentokil Initial UK Ltd	2006	Operator exposure to carbon dioxide over the course of a bubble fumigation. Not GLP / Unpublished Applicant's reference number CO2 329	Yes	ORG	No
B8.1	Rentokil Initial UK Ltd	2004	Safety Data Sheet for Carbon Dioxide dated 01/07/2004 Issue 02 / Published	No	PUB	No
B8.4	Rentokil Initial UK Ltd	2004	Safety Data Sheet for Carbon Dioxide dated 01/07/2004 Issue 02 / Published	No	PUB	No
B8.6	Rentokil Initial UK Ltd	2004	Role, Fate and Behaviour of Carbon Dioxide in the Environment Unpublished / Applicant's reference number: CO2 318	No	ORG	No
B9/01	Rentokil Initial UK Ltd	2004	Safety Data Sheet for Carbon Dioxide dated 01/07/2004 Issue 02 / Published	No	ORG	No
B9/02	Rentokil Initial UK Ltd	2005	Proposed label for Carbon dioxide/ Unpublished	No	ORG	No