Possible REACH Authorisation for ADCA

Report on Technical Support to the ADCA Task Force

20 September 2013

AMEC Environment & Infrastructure UK Limited

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Report for

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Doc Reg No. 34359CA002i3

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ISO 9001 - FS 13881
ISO 14001 - EMS 69090

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Document Revisions

No.	Details	Date
1	Draft report	06/09/13
2	Final draft report	19/09/13
3	Final report	20/09/13

Executive Summary

Introduction

This report concerns provision of technical support to the ADCA Task Force on the proposed prioritisation of ADCA for inclusion in the REACH authorisation list. It has been prepared by AMEC to enable the Task Force to provide a response to the public consultation. In particular, the work undertaken has attempted to collate better information on the use of ADCA, its supply chain and expected levels of exposure, as well as other technical issues relevant to the prioritisation of this substance. It is based primarily on the results of a survey undertaken in August 2013.

Toxicological analysis and possible safe levels

ADCA's listing on the Candidate List for proposed inclusion in Annex XIV is based on its properties as an assumed respiratory sensitiser, thereby possessing an equivalent concern with other SVHC such as CMR and PBT chemicals. At the request of the ADCA Task Force, we have undertaken an evaluation of the available toxicological data to determine whether a level of safe use could be determined. The prioritisation document for ADCA assumes that there is no threshold for effects. Current literature has been reviewed and possible safe exposure levels have been evaluated.

There is a significant amount of uncertainty in this analysis. The major data gap in both the human and animal studies is the characterisation of the sensitive subpopulation among the exposed population. Without this measure, it is very difficult to determine the potency curves. Mischaracterising individuals who will not manifest sensitisation regardless of exposure results in skewed results and high levels of experimental error.

Based on the results that are available on the respiratory toxicity of ADCA, it appears that a safe concentration of exposure can be projected to be between 0.5 and 1.5 mg/m^3 time weighted over an 8 hour work day. There are still numerous questions that need to be answered with regard to both the mechanisms of action and population heterogeneity before any statistical certainty can be attributed to these predictions. However, they are well in line with the experience in the UK where 8-hour maximum exposure limits of 1 mg/m^3 in 1996 resulted in a complete halt to reported cases of occupational asthma associated with ADCA exposure.

Supply chain and uses of ADCA

Information was collected from importers, distributors, formulators and users of ADCA in order to better understand the uses of ADCA and the related supply chains.

Information is presented in the report on the form of use of ADCA, highlighting the quantities of: ADCA powder; mixtures (i.e. pre-blended ADCA); ADCA compounds or solid master batches; liquid dispersions, paste or non dusting preparations; and other forms, including quantitative estimates of their relative importance. The report also highlights the relative importance of the different processing techniques used.

The survey covered around 12,000t of imports of ADCA, out of total imports into the EU which are estimated at around 18,000t per year. Most of the ADCA is imported in powder form, but this is often then compounded/mixed to create non-powder forms and these are the forms mainly used in downstream rubber and plastics production processes, although some of the downstream users also use the powder itself.

Of the ADCA use covered by the survey, some 50% was used in rubber articles such as flexible elastomeric insulation foam. Around 30% was used in polyolefins (used in cables, sheets and blocks), and around 20% in plasticised PVC products such as wallpaper, flooring and artificial leather. Only small quantities covered by the survey were reported as being used in unplasticised PVC, and this is considered to be an important gap in the responses received for the survey, based on the knowledge of some of the Task Force members.

Highlights of the benefits of ADCA to end product quality are provided, such as its ability to produce low-density, efficient thermal insulation foams, which provide good energy efficiency in buildings. Other benefits that ADCA foaming infers include prevention of corrosion, production of buoyant safety equipment and sound insulating properties.

Extent of use and exposure

Data were collected on the extent to which different forms of the substance are used, as this is important in determining whether (and how many) people are exposed to ADCA dust.

Based on the analysis undertaken, whilst the number of companies handling ADCA is likely to be in the order of hundreds, the number of companies handling pure ADCA is more likely to be in the region of several tens of companies.

Likewise, whilst the number of employees using ADCA or ADCA-based products is likely to be several thousand, the number of employees exposed to pure ADCA powder (assumed to have the greatest potential for inhalation exposure) is likely to be a small part of this, probably in the order of several hundred.

There are however uncertainties associated with the figures derived. The survey responses provided a good response from importers and distributors of the substance, but had gaps as regards end users, particularly users of small quantities in often-diluted form (although these are less relevant for dust exposure because plastisols/pastes without the same potential for exposure will be used).

Workplace exposure levels have also been examined, based on a relatively small dataset provided by survey respondents (which is hence subject to various uncertainties). It was not possible to collect and analyse consistent data across all of the companies concerned, but some useful information is available, highlighting that workplace concentrations of ADCA are generally higher (and more employees are potentially exposed to higher levels) where pure ADCA powder is used. The majority of workplaces where measurements were available (expressed through number of employees) had concentrations below relevant limit values such as the UK's STEL of 3 mg/m^3 and 8h-TWA of 1 mg/m^3. It is also noted that ADCA is often only part of the dust concentrations in the workplace measurements.

Whilst there was a relatively small number of respondents who reported concentrations in excess of these values, some of these data were historical and all of the companies handling the powder form reported applying forms of risk management measures that will protect workers from concentrations in the workplace environment (e.g. masks).

Information was also collected on the extent to which companies apply relevant risk management measures to protect workers. The results indicate that all of the companies responding apply at least one of the more important risk management measures that will protect workers against exposure to the dust, such as use of masks, closed systems and local exhaust ventilation / extraction. The application of such risk management measures will mean that

actual concentrations that workers are exposed to will be significantly lower than the measured concentrations in the workplace.

Details of past cases of adverse effects linked to ADCA exposure in the workplace have also been examined based on the experiences of the survey respondents, highlighting a very small number of cases of adverse health effects. These are reported to be primarily a result of improved workplace exposure controls which have been widely introduced over recent years.

Socio-economic importance and implications of (non) authorisation

The expected response of companies to a refused authorisation have been considered, highlighting that importers and distributors would need to cease trading in their activities related to ADCA.

A number of potential alternatives to ADCA have been suggested in the literature and consultation process, and respondents provided details on their suitability for different applications on technical, economic and health/environmental grounds.

Overall, whilst the majority of respondents acknowledge there may be some, limited applications where substitution may be possible, albeit with some loss of product functionality/quality, the consensus amongst those consulted was that there is no technically suitable alternative to ADCA without an unacceptable loss of functionality/quality or global competitiveness. Concerns were also expressed that the use of alternatives could potentially introduce risks arising from substances that are less thoroughly tested, through the (eco)toxicological impacts that they may pose, as well as through inferior product performance.

The implications of this are that much of the ADCA-foamed articles currently on the market could no longer be produced in the EU, and a significant proportion of this use could be replaced by imports from outside the EU, where ADCA could presumably still be used as the authorisation process does not apply to use of articles.

The report provides an analysis of the potential scale of business closures, lost turnover, employment and wider economic impacts, which are substantial.

Findings

The report includes a range of information that is likely to provide an improved understanding of the use of and exposure to ADCA in the EU. In order to support the ADCA Task Force with providing a response to ECHA's public consultation, some conclusions are drawn on the potential implications against the criteria used in the prioritisation approach used to select substances for inclusion in Annex XIV.

Possible alternative scores have been provided taking into account the new information obtained through the survey as well as the fact that REACH registrations have recently been amended to remove registration of all consumer and professional use, and to remove certain industrial applications considered in the prioritisation process (e.g. industrial spraying) which, if they took place, could have led to more significant exposure.

Overall, these data suggest that the numbers of workers exposed to the more toxicologically relevant form of ADCA (powder) are likely to be much lower than the total number of people handling the substance, most of which is in non-dusting form. Furthermore, relevant risk management measures seem to be widely applied amongst the industry respondents, suggesting that exposure may be better controlled than assumed in the prioritisation process (which was partly based on now-superseded information). This suggests that, taking into account the scoring and prioritisation process for inclusion of candidate list substances on Annex XIV,

ADCA could be a significantly lower priority for inclusion than the previously available data suggested.

The report also summarises other relevant aspects taken into account in the prioritisation process, such as geographical distribution of supply chains, the presence of (or potential for) specific EU legislation other than authorisation and the regulatory effectiveness of a possible authorisation requirement.

Contents

1. Introduction

1.1 Scope

This report concerns provision of technical support to the ADCA Task Force on the proposed prioritisation of ADCA for inclusion in the REACH authorisation list.

Following submission of an Annex XV dossier by Austria, in December 2012, the Member State Committee adopted a supporting document for the identification of diazene-1, 2-dicarboxyamide (ADCA) (CAS Number: 123-77-3; EC Number: 204-650-8) as a substance of very high concern (SVHC) based on its properties as a respiratory sensitiser. ADCA was included in the Candidate List for authorisation in December 2012.

Following a prioritisation process, ADCA has been included in the European Chemicals Agency (ECHA) latest recommendation for inclusion in the REACH authorisation list[1]. A public consultation related to that prioritisation was launched by ECHA on 24 June 2013, to run until 23 September 2013.

AMEC Environment & Infrastructure UK Limited (AMEC) has provided technical support to support the ADCA Task Force, a group of some 50 companies who import/distribute ADCA or use it in their operations in the European Union, to enable them to provide a response to the consultation. In particular, the work undertaken has attempted to collate better information on the use of ADCA, its supply chain and expected levels of exposure, as well as other technical issues relevant to the prioritisation of this substance.

Relevant technical information has been collected through an extensive survey of task force members (and some of their customers[2]) over approximately three weeks in August 2013. Further details on the membership of the task force and the survey are set out in Annex 1.

The responses to the survey questionnaire have been prepared by each individual company based on its own, individual judgment and without discussing these with other companies. This report contains confidential information and should not be made public.

1.2 Contents of this Report

Following this introduction:

- Section two provides an evaluation of the status of ADCA as a sensitiser, based on currently available information and considers available toxicological data to determine whether a level of safe ADCA use could be determined. The fact that ADCA has harmonised EU classification as a respiratory sensitiser is not questioned/disputed.

[1] http://echa.europa.eu/addressing-chemicals-of-concern/authorisation/recommendation-for-inclusion-in-the-authorisation-list/-/substance/4108/search/+/term

[2] The total number of companies responding to the survey was >80, as some responses were received through customers of the Task Force members.

- Section three sets out details of the supply chain and provides clarification on current uses of ADCA.
- Section four examines the extent of use and exposure to ADCA. This draws on data on the numbers of sites and numbers of workers exposed, alongside the risk management measures in place, as well as exposure levels (especially exposure to powder versus other forms).
- Section five examines the key socio-economic importance of ADCA and implications of possible (non) authorisation.
- Findings are provided in chapter six.
- Annex 1 contains additional details of the survey noted above; Annex 2 contains references to the literature referred to in the toxicological assessment.

This is a final report on the study, taking into account comments received from Task Force members on the drafts of 6 September and 19 September.

2. Toxicological Analysis of Possible Safe Exposure Levels for ADCA

2.1 Introduction

ADCA's listing on the Candidate List for proposed inclusion in Annex XIV is based on its properties as an assumed respiratory sensitiser, thereby possessing an equivalent concern with other SVHC such as CMR and PBT chemicals. At the request of the ADCA Task Force, we have undertaken an evaluation of the available toxicological data to determine whether a level of safe use could be determined. The prioritisation document for ADCA assumes that there is no threshold for effects.

This section provides a brief review of current studies and reports related to the respiratory impacts of ADCA. This is followed with an analysis of the best estimates of impact probability based on current data. The final part of this document discusses the current data gaps in our understanding of ADCA respiratory toxicity and suggests ways that the data gaps could be possibly addressed. References are provided in Annex 2.

2.2 Current Literature on ADCA Toxicity

2.2.1 Overview

The following is a brief description of the current literature on the respiratory impact of ADCA. Animal studies are reviewed first, followed by human epidemiological studies and lastly reviews/analyses. Included in the epidemiological studies are case studies. Unfortunately, the case study reports do not provide usable data beyond that for the precise individuals described. The reason for this is two-fold. First, case study reports provide no control and rarely any usable exposure statistics. Therefore the relation between the reported syndrome and the cause is almost always alleged. Second, the individuals are almost always grouped based on the manifestation of an adverse effect. While useful when comparing and contrasting the nature and progression of the effect, it does not provide information to express the etiology in a quantitative manner. To do this, the individuals must be grouped based on experiences, not outcomes. Therefore, there are several limitations to defining ADCA sensitivity based on case studies.

Throughout the publication period of these articles, the definition of "Occupational Asthma" has evolved, particularly with the identification of Reactive Airway Dysfunction Syndrome (RADS) as being different from adult onset asthma. RADS was not formally recognised as a distinct disease state until 1985 and was therefore not considered in any of the epidemiological studies available on ADCA. While RADS is usually only moderately chronic with symptoms lasting from several months to a couple of years, adult onset asthma is chronic and irreversible (Walusiak 2006). Definitive identification of asthma requires demonstrable reversal of reduced vital capacity through the administration of a ß-agonist.

Particular emphasis should be placed on the studies of Slovak 1981 and Whitehead et al. 1987. These are the principal studies upon which ECHA's Support Document for Identification of ADCA relied.

2.2.2 Animal Studies

Ferris et al., 1977

An occupational epidemiological study was completed at a company that grinds various materials including herbicides, nylon tertpolymers, aluminum oxide, sulfanilamide, amorphous silica and fibreglass into fine powders ranging from 2 to 10 µm. Shortly after azodicarbonamide (ADCA) was added, workers on the day and night shifts complained of "colds" and "pneumonia" characterized by increased temperatures, pains in the chest and productive coughs. Forced vital capacity (FVC) and forced expiratory volume (FEV_1) were measured in workers and were found to be lower than occupational groups that are not exposed to pulmonary irritants. Although this preliminary study calls attention to the possible pulmonary reactivity of inhaled finely ground ADCA to which small numbers of workers may be exposed, this study did not evaluate whether the other grinding materials were associated with these symptoms.

Gerlach et al., 1989 (used for REACH registration)

Two groups of male Hartley guinea pigs were exposed six hr/day, five days/week for four weeks to aerosolised ADCA at 51 or 200 mg/m^3 or to filtered air as controls. One group was tested for specific sensitisation to ADCA by measuring specific airway conductance during inhalation challenge with ADCA before and on the third day after the four-week ADA exposure. The other group was tested for non-specific airway sensitisation by inhalation challenge with aerosolised histamine before and after the four-week ADA exposure. Histamine was administered in stepwise increasing concentrations to elicit an airway response in each guinea pig. Body weight and histopathology of the respiratory tract were evaluated. The four-week exposure to ADCA did not result in either specific or non-specific airway sensitisation nor were there positive skin reactions, influences in body weight or histopathological responses. The results of this study do not support the role of ADCA as either a specific or non-specific pulmonary sensitiser when inhaled by the guinea pig without prior conjugation to a protein. Additionally, the authors further conclude that it appears unlikely that single exposures of normal, naïve humans to ADCA alone would cause symptoms of airway irritation but does not preclude the possibility that specific sensitisation, particularly for sensitive subjects, might display irritant response or nonspecific sensitisation to inhaled ADCA.

A limitation of this study stems from assumptions of treatment homogeneity. Standard errors in excess of 50 percent of the respiratory measures were not uncommon in their data set. Fortunately, as part of the post-sensitisation ADCA challenge experiment, the authors indicated that at 50 mg/m^3 exposure, two of the animals showed marked and different responses compared to the other eight in the treatment group. This could very well be an indication of the population heterogeneity.

Shopp et al., 1987

The purpose of this study was twofold. The first purpose was to determine the level of ADCA that would result in acute adverse effects on guinea pig pulmonary structure and function, and secondly, to select exposure levels and nonirritating challenge levels for use in future studies assessing the sensitising potential of ADCA in the guinea pig.

Groups of 20 guinea pigs were exposed to each of three concentrations of ADCA (19, 58, and 97 mg/m^3) plus air as a control for one hour. Pulmonary function was measured before exposure, during exposure, immediately after exposure, and 24 hours after exposure. Dynamic compliance (C_{dyn}), total pulmonary resistance (R_L), tidal volume (V_T), respiratory frequency and minute volume were measured along with gross necropsies and histological examination of

respiratory tract tissues conducted immediately following the exposure or 24 hours after exposure. There were no effects of ADCA exposure on gross necropsy, histology, C_{dyn}, or R_L. Some significant, concentration-related decreases in V_T, respiratory frequency and minute volume were seen; however, the magnitudes of these changes were small. The largest change was seen in minute volume, amounting to a 24% decrease in the high concentration group. Inhalation exposure of guinea pigs to ADCA at concentrations up to 97 mg/m^3 (i.e. 50x concentration detected in occupational settings) resulted in minor changes in pulmonary function without any changes in lung histology. The authors conclude that ADCA is an upper airway irritant because the C_{dyn}, and R_L values were unchanged.

Since the protocol used in this study would not have revealed functional changes due to sensitisation, this paper cannot be used to support the sensitising potential of ADCA.

2.2.3 Human Epidemiological Studies

Slovak, A., 1981

A prevalence study of occupational asthma was conducted using a questionnaire among a group of 151 workers who had been or were exposed to ADCA dust during manufacture. (Workers were between 29 and 63 years old with a mean age of 41. Approximately 43% of the population were smokers and another 32% were ex-smokers (>1 year) and 25% were life-time non-smokers.)

The author diagnosed "asthma" as a history of repeated episodes of wheezing or chest tightness (+cough) related to exposure to ADCA. Using medical notes made at the time of the attacks, asthma was diagnosed in 12 of 28 cases. It was determined that the 8-hr time-weighted average (TWA) concentrations were between 2 and 5 mg/m^3.

The prevalence of ADCA-induced asthma was 18.5%. The questionnaire determined that over 50% of the patients developed asthma within three months of the first exposure and 75% within the first year. The predominant symptoms were shortness of breath, chest tightness and wheezing. Other symptoms included cough, rhinitis, conjunctivitis, and rash.

Spirometry was performed on three groups of people from the total worker population which included persons diagnosed with ADCA-induced asthma, all asymptomatic process workers in daily exposure who were at the plant for more than one year, and a control process worker population without any contact with ADCA or other lung sensitizers. FEV_1, FVC, and FEV_1/FVC ratio were recorded. There was no evidence of reversible airflow obstruction and no attacks were observed during the study. The groups tested had an excess of atopics in both groups compared to the general population.

The author suggests caution must be exercised in the conclusions drawn in sensitised workers from pre- and post-shift spirometric data. The pre-shift reading cannot be taken as a true unaffected baseline since the airways may still be maximally constricted from previous exposure. Similarly, the absence of a drop over as shift cannot be taken as evidence of absence of an effect.

The author concluded that the results suggest that ADCA can be viewed as a potent lung sensitiser of the small molecular weight type with a predominance of severe and worsening late onset asthmatic symptoms usually occurring within the first year of exposure.

This investigation is based on a retrospective questionnaire. The threshold for the diagnosis of occupational asthma was very low and based exclusively on subject recall and often in conflict

with lung function tests that were all negative. The study also had no controls and did not provide a timeframe for the subjects, meaning that atopic adult onset asthma could not be discerned from any ADCA-dependent conditions and no long term follow-up to distinguish adult onset asthma from RADS. Additionally, the exposure concentrations cited in the study were not substantiated making the resulting potency relations highly uncertain.

Whitehead et al., 1987

Respiratory health variables were studied cross-sectionally in 227 employees of a plastics molding facility where numerous complaints were seemingly associated with the use of ADCA in injection molding. The tests did not demonstrate statistically significant differences when stratified by smoking status and work status with respect to injection molding. Symptoms included irritation, cough, wheezing, and headache and were significantly more prevalent in injection molding than all other departments. ADCA concentrations ranged from 0.001 to 0.752 mg/m^3 with a mean for the injection workers of 0.0361 mg/m^3.

Pre- and post shift respiratory status measures and ADCA concentrations were obtained for a small group of employees. Cross-sectional pulmonary function differences were not observed. Modest decrements in pulmonary function measures were observed between the beginning and end of shift but with no dose-effect relationship. Symptom causation may be some combination of ADCA itself, reaction products of ADCA formed during injection molding, or other unidentified agents uniquely associated with the process of injection molding with ADCA foaming agent. This project could not identify conclusively which cause(s) are active.

Although observations were controlled between the unexposed and exposed groups, the rate in the control group was 50 percent of the treatment, meaning that half of the impact was in fact atopic with regards to ADCA exposure. The principal weakness with this study was the application of the statistical measures across the entire exposed population (i.e. assuming population is uniform and random). Because the model used had an underlying assumption that the population was homogeneous (when it is known that sensitivity to occupational asthma is not), there was, as a result, massive levels of variability in their measurements resulting in no detectable dose response.

Kim et al., 2004

The first case of occupational asthma due to ADCA reports a 56-year-old man with cough, dyspnea, and wheezing. He worked at an ADCA manufacturing plant where he performed quality assessment on finely ground ADCA. Symptoms appeared seven years after he started working. He was evaluated at a hospital resulting in no medical history other than smoking a half-pack of cigarettes per day for 20 years. An inhalation challenge was performed with ADCA and lactose powder as the control. On day 1, the patient was asked to move 30 g of lactose powder for 10 minutes which resulted in no significant change in FEV_1 over the next seven hours. On day 3, the challenge consisted of 50% lactose powder and 50% ADCA for 10 minutes. FEV_1 was measured five hours after exposure and it decreased 22.4% with complaints of cough and chest tightness which was not a significant change. Nonspecific bronchial hyperresponsiveness increased after the inhalation challenge. The authors indicated that the patient demonstrated typical features of occupational asthma similar to those described in other studies; a strong relationship between work and asthmatic symptoms, presence of a latency period, worsening of symptoms at the end of the day's work or in the evening and characteristic late-phase response to inhalation challenge.

The authors postulate that the late-phase response is probably driven by immunologic mechanisms, especially T-cell immunity rather than IgE-mediated immunity, and may be

involved in the development of ADCA-induced occupational asthma. Furthermore, the authors cite studies where ADCA was shown to be a T-cell immunosuppressant *in vivo* and *in vitro*. Studies have shown that ADCA inhibits both the proliferative response of CD4+ T-cells and their secretion of IL-2, IFN-λ, IL-4 and IL-5, and these inhibitory actions may have a negative effect on the development of ADCA-induced asthma. The immunosuppressive effects are displayed in a dose-dependent manner and relatively large amounts are required to exert T-cell immunosuppressive action (several grams/day orally in humans). Thus, this activity may not be applicable to the inhalation pathway.

Normand, et al., 1989

Four case studies were summarized involving workers exposed to ADCA. All cases involved men from 45 to 54 years old who worked in plastics factories grinding various materials including ADCA. All four workers exhibited symptoms of asthma. After the first contact and a short period with no signs, the attacks appear suddenly, generally within six months of exposure, and 75% of the cases occurred before the end of the first year. The attacks happened with delay at the end of the day's work or late at night.

Specific inhalation tests using ADCA were conducted measuring FVC and FEV_1 in Workers 1 and 2 resulting in lower than predicted values. In all cases, the asthma attack disappeared after exclusion of the ADCA or changes in working conditions and reappeared only after an accidental or controlled medical re-exposure.

The authors state that they cannot totally exclude the possibility that substances other than ADCA were implicated in the cases described however, the inhalation challenges performed with the ADCA used by the two workers and the clear association with the use of ADCA in the other two subjects strongly point to ADCA (or possibly a contaminant) as the causative agent.

Case 4 in the report showed only transient response to ADCA that improved with time suggesting that the original cause of the reported reduced FEV was likely due to RADS as opposed to adult-onset asthma.

Vaniniotalo & Pfäffli, 1988

This study determined ADCA concentrations in occupational settings during extrusion, blowing, injection molding, and spread coating. The resulting airborne concentrations ranged from 0.0025+0.0001 mg/m^3 to 17.5+7.2 mg/m^3. It was noted that when dry ADCA decomposes, it produces gases (32%), solid residues (41%) and subliming substances (27%); the gases comprise nitrogen (65%), carbon monoxide (32%) and carbon dioxide (3%). Further, when heated, some of the ADCA may sublime without decomposing and enter workplace air.

2.2.4 Other Studies

WHO, 1999

This document is based on a review of human health, primarily occupational, concerns from the United Kingdom's Health and Safety Office. The literature search covers up through 1997.

Toxicokinetic data indicate ADCA is well absorbed via inhalation (~34%) and oral (~10-33%) routes in rodents. It is readily converted to biurea and it is likely that systemic exposure is to this derivative rather than the parent compound. The conversion to biurea takes place in the presence of thiol groups. It is of low acute toxicity and does not cause skin, eye, or respiratory tract irritation in experimental animals. "Results from a poorly conducted skin sensitization study were negative, and there was no evidence of an asthmatic-type response in guinea pigs in

one study". No adverse effects were observed in experimental animals inhaling up to 200 mg/m^3 for up to 13 weeks.

Studies in humans have concentrated solely on the ability of ADCA to induce asthma and skin sensitisation. Evidence of such has been found from bronchial challenge studies with symptomatic individuals and from health evaluations of employees at workplaces where ADCA is manufactured or used.

Data obtained by the UK HSE showed average personal exposure during the day shift to be 9.8-11.8 mg/m^3 and 2.3-2.8 mg/m^3 at micronising mills (sample collected over 4 hours).

WHO states that for irritation and sensitisation, "most studies were of uncertain quality and in many cases would not comply with modern regulatory standards, results of several skin and eye irritation studies indicate that azodicarbonamide should not be regarded as a skin or eye irritant". WHO cites the results of Shopp et al., 1987 that "no changes or effects of doubtful significance were reported for various lung function parameters, indicating that irritation was minimal at concentrations up to 97 mg/m^3 for 1 hour". Gerlach et al. (1989) was also discussed as having "no evidence of pulmonary irritation or asthmatic-type reactions…, no evidence of histopathological effects on the upper or lower respiratory tract, and no evidence of circulating antibodies…".

For humans, WHO cites two studies (Malo et al., 1985; Pineau et al., 1985) with the "strongest evidence" for workers alleging asthma inducted by exposure to ADCA. Two individuals (one atopic, one non-atopic) who worked at the same factory and were intermittently exposed (i.e. 1-2 weeks duration, 3-4 times/year) were evaluated. A few months after first exposure to ADCA, symptoms developed and described as "eye/nose irritation" at work, followed by a few hours later by nocturnal asthmatic symptoms. After one month free of ADCA exposure, both subjects underwent lung provocation studies using lactose (control); 50:50 mixture of lactose/ADCA and ADCA for 10 seconds on the next day. On both days, lung function was monitored. After the ADCA challenge, the atopic individual developed a late respiratory response starting three hours after challenge and reaching a maximum 24% drop in FEV_1 at six hours after challenge. It did not return to normal until six weeks after challenge. The non-atopic individual showed a dual response with peak reductions in FEV_1 of >20% recorded 30 min and 5-6 h after exposure. Six other cases (Valentino & Comai, 1985; Alt & Diller, 1988; Normand et al., 1989) provided less robust evidence that ADCA was the cause of respiratory symptoms.

WHO indicated that the study by Whitehead et al. (1987) and Ahrenholz & Anderson (1985) showed no clear differences in the result of lung function studies between those exposed to ADCA and non-exposed individuals. Air sampling showed that the highest concentration of ADCA recorded was 0.01 mg/m^3; however, toluene, styrene, phenols, and triphenyl phosphate were also detected at concentrations at or below the odor threshold for each substance. Symptoms were reduced when ADCA was removed.

For inhalation sensitisation, WHO concludes that ADCA is an "asthmagen" owing to the evidence of a link between ADCA and respiratory problems. However, there is no information available relating to dose-response relationships or levels associated with the induction of a hypersensitive state or provocation of an asthmatic response. Hence, it is not possible to reliably quantify the risk of developing occupational asthma.

Rodford et al., 2003.

There are no well-established tests for respiratory sensitization potential so the authors suggest the use of quantitative structure activity relationship (QSAR) modeling. The relationship

between structure and electrophilic potential was investigated for the development of SAR models for chemical allergens using computer automated structure evaluation (CASE) (MultiCase, Beachwood, OH, USA) systems. ADCA was one of 40 chemicals documented to elicit a >20% decrease in FEV_1 at one second within 24 hours of an inhalation provocation challenge. Additionally, the model imposed a chemical size restriction (i.e., at least two contiguous non-hydrogen atoms) and the exclusion of metals. The model identified the isocyanate grouping (N=C=O), primary and secondary amines, substituted aromatic moieties and distance descriptors. Respiratory sensitizers were also found to differ from non-sensitizers in certain physicochemical properties, including molecular weight, water solubility, log K_{ow} (octanol-water partition coefficient), and the lowest-unoccupied molecular orbital. When modeled using Bayes' theorem, ADCA was predicted to be "active" and the MultiCase submodel predicted medium likelihood of being a sensitiser.

2.3 Evaluation of Safe Exposure Levels

2.3.1 Overview

This section provides an analysis of the data available in the above studies and evaluates the information to determine a safe use level. The section starts with a brief review of occupational asthma as a toxicological endpoint. The relative toxicity is then analyzed with regards to dose response and probability of impact based on available observations. The final section outlines the current data gaps and recommendations for studies that may be used to fill the information gaps.

2.3.2 Occupational Asthma

Adult-onset (or late-onset) asthma is considered when asthma symptoms represent for the first time during adulthood. Several definitions of adult-onset asthma can be found in the literature. The age at diagnosis determining the term late-onset asthma varies from 12 years of age to ≥65 years of age. Asthma that starts in adulthood differs from childhood-onset asthma in that it is often non-atopic, more severe and associated with a faster decline in lung function. The incidence among adults is as high as 12 cases per 1,000 person-years. The estimated adult incidence of asthma from pooled general population studies appears to be 4.6 cases per 1,000 person-years in females and 3.6 in males, and there is a trend towards a higher incidence with age. Although there are several risk factors, triggers and co-morbid conditions[3] associated with incident asthma in adults, we will be discussing asthma related to sensitising or irritant exposure in the workplace (as it relates to ADCA) for the duration of this report.

Work-related asthma (WRA) is a broad term that refers to asthma that is exacerbated or induced by inhalation exposures in the workplace. WRA includes occupational asthma (OA) that refers to de novo asthma or the recurrence of previously quiescent asthma induced either by sensitisation to a workplace substance, termed sensitiser-induced OA, or by exposure to an inhaled irritant at work, termed irritant-induced OA. Estimates of the incidence and prevalence of OA vary. It has generally been accepted that at least 9% to 15% of adult asthma can be attributed to workplace exposures, although recent data indicate that 25% or more of de novo asthma may have an occupational basis. Failure to recognize OA in a timely fashion can lead

[3] Risk factors, triggers and co-morbid conditions other than asthma related to sensitising or irritant exposure in the workplace include: environmental pollutants; female sex hormones; upper airway diseases; aspirin and paracetamol intake; respiratory infections; obesity; and stressful life events.

to permanent respiratory impairment, underscoring the need for early diagnosis and intervention.

Sensitiser-induced asthma is a subtype of occupational asthma typically presenting with a latent period of exposure, followed by the onset of clinical disease. After sensitisation, airway reactions develop from levels of exposure to the sensitising agents that were tolerated before sensitisation. Although the mechanism causing occupational asthma from some sensitisers has been demonstrated to have an immunological basis (IgE mediated or otherwise), the mechanisms for some suspected sensitisers are yet to be defined. There are more than 250 agents that have been adequately documented to cause sensitiser-induced asthma. Some sensitising agents have differential effects on asthma onset depending on the dose.

Irritant-induced asthma is a subtype of occupational asthma without immunological sensitisation and includes the typical reactive airways dysfunction syndrome and a more gradual form called not-so-sudden irritant-induced asthma, when asthma follows repeated low-dose exposure to irritants.

The prognosis of occupational asthma depends primarily on cessation of exposure to the offending agent, the duration of exposure to sensitisers, and the severity of asthma when diagnosed. Timely removal of workers from exposure to a sensitiser causing OA is generally associated with favorable outcomes. Prolonged follow-up may be required to ascertain outcomes in any individual, particularly in OA from sensitisers in which there may be continued improvement of lung function for 2 years or more after exposure ends.

2.3.3 Relative Toxicity of ADCA

AMEC examined three separate toxicological models to determine which provided the best success by indicating a relation between exposure and response. They were as follows:

- Standard dose response analysis over general population of exposure;
- Probability exposure/impact model over the general population of exposure; and
- Probability exposure/impact model within the block/cohort of sensitive subpopulation(s).

Dose Response

None of the animal studies provided a positive gradation of impact with increasing amounts of exposure. This may represent a significant data gap. However, dose response may not be the most appropriate model for the evaluation of bronchial hypersensitivity as a toxicological endpoint. Conditional endpoints such as sensitisation, like cancer, cannot be graded on a continuous scale of severity because either factors inherent to the test subject or random uncontrolled factors related to the disease state's progression swamps out any relation between dose and degree of response. A chemical can be qualified as a weak or a strong carcinogen, but the resulting disease state cannot be characterised as a mild cancer or a severe cancer. Similarly with sensitisers: the rate of immune memorization induction quantifies a sensitiser as being either weak or strong based on the probability of impact. The severity of the immune response, either as an induced inflammation or a hyper-sensitisation such as atopic asthma, is a function of the affected individual's signal transduction efficiency and the magnitude of the manifest afferent response by the target cells. Hence, for a mechanistic point, dose response does not represent the best method of analysis. Clearly, it is the discontinuous determination of the likelihood of disease state induction that better fits this type of toxic endpoint.

Probability of adverse effect (general population)

Of all the studies reviewed, three provided data from which possible probability determinations could be made: the guinea pig study by Gerlach et al. (1989) and two cross-sectional epidemiology studies by Slovak (1981) and Whitehead et al. (1987). Unfortunately, the case study reports do not provide usable data beyond that for the precise individuals described. The reason for this is two-fold. First, case study reports provide no control and rarely any usable exposure statistics. Therefore the relation between the reported syndrome and the cause is almost always alleged. Second, the individuals are almost always grouped based on the manifestation of an adverse effect. While useful when comparing and contrasting the nature and progression of the effect, it does not provide information to express the etiology in a quantitative manner. To do this, the individuals must be grouped based on experiences, not outcomes.

It should be noted that some assumptions had to be made and the resulting analyses demand that such assumptions are true for the projections to be valid. Unfortunately, based on the quality of the data, this was necessary. Details are provided in the uncertainty section.

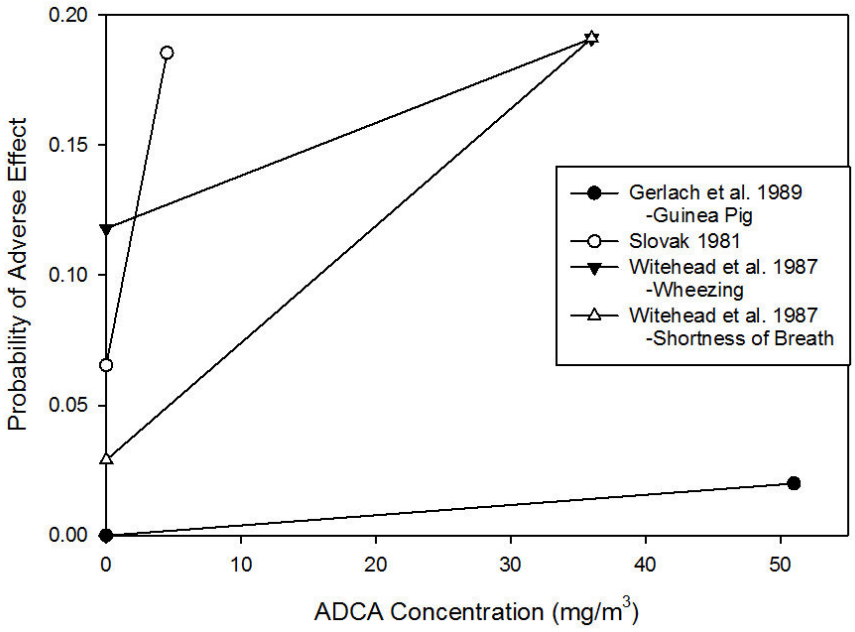
In the three studies, we examined the relative slope of a relation between the reported control populations exposure dose where the probability of response (P(r)) was modeled as a 4-parameter Chapman relation as follows:

$$P(r) = P(r)_{x=0} + P(r)_{\max} \cdot \left(1 - e^{-\beta x}\right)^{c}$$

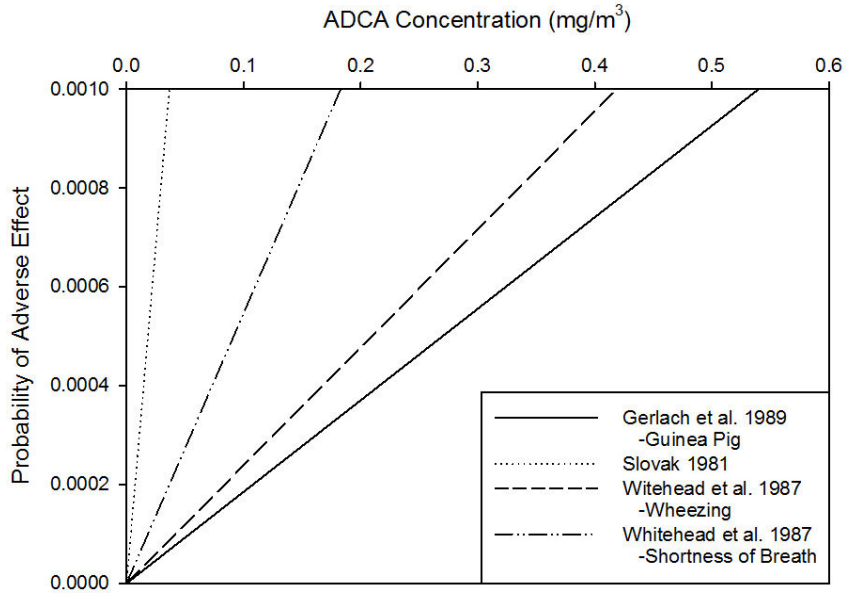
Where P(r)max is equal to a maximum probability of impact of 1 and the exposure concentration (x) is the suspended airborne concentration, time-weighted over an 8 hour exposure period.

In all three of these cases, the resulting potential indication of respiratory impact was at the lowest exposure concentrations. This unfortunately results in a 2-point regression that is very uncertain (i.e. c=1). However, mechanistically the uncertainty will be conservative in that it will automatically assume linearity to the origin and defaults to an exponential rise to a maximum of 1 or 100 percent probability of impact. Unfortunately, it also does not permit the elucidation of a no observed adverse effect level (NOAEL). Hence, it will be necessary to define subjectively a level of allowable impact.

The relative relations from the three studies are provided below. Note that the endpoint used in the interpretation of the Gerlach et al. (1989) study was the proportion of guinea pigs that responded to the post exposure challenge (2/10) and not the magnitude of the response. The response in the Slovak (1981) study was self reported with an assumed constant ADCA exposure between 2 and 5 mg/m^3. Whitehead et al. (1987) only confirmed ATS symptoms were considered and those most specific to asthma (wheezing and shortness of breath).



Selecting a safe level of exposure is a management decision and not a toxicological one. For illustration purposes, and considering the low proportion of the total population likely to ever work in an occupation that would result in exposure to ADCA in a respirable form, we selected an allowable of 1 in 1,000 exposures. Using the potency factors derived from the above relations, allowable 8-hour time-weighted concentrations for ADCA were determined as illustrated below:



	ß $(mg/kg\text{-}day)^{-1}$	[C] at P = 0.001mg/m^3
Slovak 1981	0.289	0.0365
Whitehead et al 1987 (shortness of breath)	0.0517	0.183
Whitehead et al 1987 (wheezing)	0.0226	0.419
Gerlach et al. 1989 (Guinea Pig)	0.0260	0.540

The results indicate about a 10-fold range between the minimum estimate based on Slovak (1981) and results of Whitehead et al. (1989) for wheezing. Interestingly, the results of Gerlach et al. (1989) fall in about the same range as Whitehead et al. (1987).

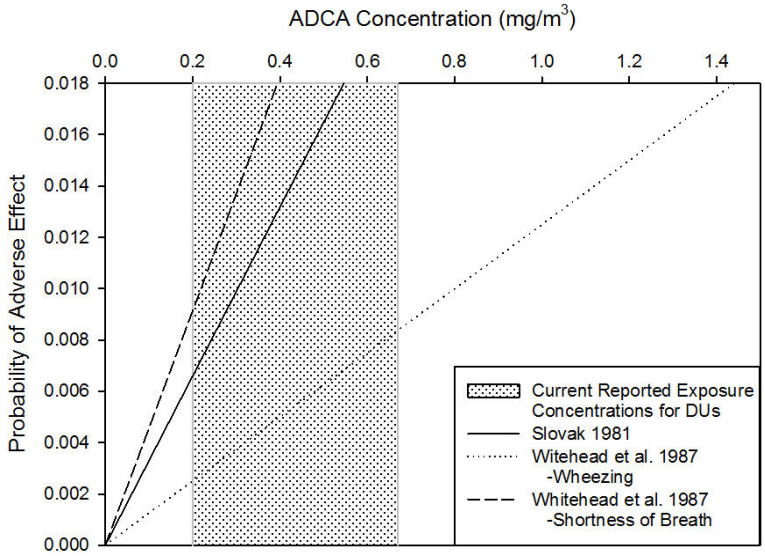
The results of Slovak (1981) were based on a retrospective questionnaire given to the workers. Of the 28 reporting asthma-like symptoms, less than half of them had any contemporary documentation and none had any atopic diagnoses. The study also had no controls and in situ challenge showed no negative effect on airway resistance.

Probability of adverse effect (Target population)

The above analysis inherently assumes that all members of the exposed population have the same dose-dependent probability of incurring the adverse effect (occupational asthma). However, when it comes to sensitisation, this does not appear to be the case. There appears to be determinants within the population that make individuals more susceptible to sensitisation through immune system memorisation than others. Some portions of the population may be incapable of forming the type IV memory of ADCA and thus the exposure can be increased to otherwise toxic levels with no immunity-based response. Combining these two populations in a study can result in high variability within treatment groups resulting in accepting no impact when in fact there was an impact. The issue in a population that demonstrates a heterogeneous response such as this is not the magnitude of the response across the population, but the magnitude of response in sensitive (i.e. impacted) individuals. Statistically speaking, the population needs to be considered within a randomised complete block design where the exposure rate is considered the treatment and the proportion of sensitive individuals within the treatments are considered the blocks.

Radical heterogeneity as seen with sensitisation reactions introduces a secondary and independent probability to the system and that is the chance that a sensitive individual will be put into a position whereby they will come into contact with ADCA in concentrations sufficient to elicit a response. Often this can be overcome through the assumption of high population exposure over long period of time. This will likely significantly over predict the response because: 1) situations of ADCA exposure are rare among the general population, and 2) there is an insignificant background rate of adult onset asthma. It has been estimated that the probability of suffering adult onset asthma is 3.8 per 1,000 individuals per year with about 25 percent of that attributable to workplace causes (Dykewicz 2009). This means that, over a working career of 45 years, one would expect a 12.8 percent atopic adult onset asthma rate within the population with a 9.5 per 10,000 individuals who are both sensitive and exposed to an occupational sensitizer.

The data was reanalyzed with an assumption of 20 percent (P(s)) sensitivity to sensitisation (based on reasonable maximum response within the data) and a spontaneous atopic rate within this population of 2.7 per 500 individuals (P(a)). The probability of an individual working in an exposing environment (P(x)) was assumed to be random and therefore equal to the proportion of the total population (P(xls) = 20%). If we assume that 75 to 80 percent of the sensitisation to ADCA occurs within a year (as suggested by both Whitehead et al. 1987 and Slovak 1981), then the probability of occupational asthma (P(o)) exceeding the atopic rate can be defined (0.75P(a)) The result is that the effective P(o) within the sensitive population corresponding to a P = 0.001 in the general public would be 0.018 mg/m^3 as illustrated below:



	ß (mg/kg-day)$^{-1}$	$[C]_{max}$ for P(o) > P(a) mg/m^3
Slovak 1981	0.347	0.546
Whitehead et al 1987 (shortness of breath)	0.486	0.394
Whitehead et al 1987 (wheezing)	0.131	1.44

The graph above provides an overlay of current reported minimum and maximum reported occupational exposure concentrations of inhalable ADCA (WHO definition) from downstream users (DUs) in the plastics industry[4].

2.3.4 Uncertainty and Data Gaps

It is unfortunate that there is a significant amount of uncertainty in this analysis. There are two principal aspects in this case. First, the available epidemiological studies date from the 1980s. While this is no reason to doubt the studies' observations, they are handicapped by antiquated methods of statistical analyses and outdated clinical interpretations of signs and symptoms. Even the definition of "Occupational Asthma" has evolved over this time particularly with the

[4] ADCA Task Force comments on the proposal of Austria for identification C,C-azodi(formamide) (ADCA) as a Substance of Very High Concern. Submitted as part of the public consultation in 2012.

identification of other chronic respiratory conditions such as Chronic Obstructive Pulmonary Disease (COPD). COPD is inflammatory and not immune based. Early signs of COPD may mimic asthma (Quaseem et al. 2011). For example, one of the cases examined by Normand et al. (1989), an ex-smoker and alcoholic with a history of previous work in the melamine formaldehyde industry, showed classic COPD symptoms (FEV:FVC < 0.7) that was taken by the authors as ADCA-induced asthma. Definitive differentiation can be accomplished through pulmonary x-rays. Since this was not done in any of the studies, it is not possible to ensure that all of the cases identified as asthma were in fact asthma.

As discussed earlier, another potential for misdiagnosis was mistaking RADS for asthma. RADS was not formally recognised as a distinct disease state until 1985 and was not considered in any of the epidemiological studies available on ADCA. The principal differentiation between RADS and asthma is long term prognosis: RADS is usually only moderately chronic with symptoms lasting from several months to a couple of years, whereas asthma is chronic and irreversible (Walusiak 2006). Also noteworthy is the differentiation in the manifestation of the bronchial reactivity. In asthma, inflammation appears secondary to the bronchial constriction with both being manifest after a variable lag phase. Contrarily, in RADS the inflammation appears to be primary and precedes bronchial constriction. This was seen in one of the subjects in the case study presented by Malo et al. (1985). Subject B in this case showed very rapid onset with a secondary later onset. This is unusual for asthma where reductions in FEV tend to be relatively linear reaching effective resistance in 60 to 120 minutes. Likewise, Case 4 in the report by Normand et al. (1989) showed only transient response to ADCA that improved with time suggesting that the original cause of the reported reduced FEV was likely due to RADS as opposed to adult-onset asthma.

It appears that RADS may be more closely related to exposure to irritant agents and does not require an immunosensitisation component. This hypothesis however is still under contention and it is unclear whether or not RADS has a Type IV allergic component.

The second concern regarding the age of the available studies on the impact of ADCA exposure is that the occupational exposure models described do not represent current production practices as they have changed over the intervening 26 years.

Another issue related to uncertainty in this analysis is that the published results and statistics that could be used in the development of dose-response probability relations were in a form that was not germane to probabilistic analysis. This was most likely due to changes in quantitative epidemiology that have occurred since their publication. Our principal concern is with regards to the methodology applied by Slovak (1981) in his retrospective questionnaire-based study. The threshold for the declaration of occupational asthma was very low and based exclusively on subject recall. Lung function tests were all negative meaning that there was no objective data supporting the questionnaire. The study also had no controls and did not provide a time frame for the subjects, meaning that atopic adult onset asthma could not even be predicted. Furthermore, the exposure concentrations cited in the study appear to have no basis, therefore making the resulting potency relations highly suspect.

The study by Whitehead et al. (1987) provided a better quality of data. Observations were controlled between the cohort that worked with ADCA and those that did not. As a result, while the rate of chronic wheezing in the ADCA group was comparable to that reported by Slovak, the rate in the control group was 50 percent of the treatment, meaning that half of the impact was in fact atopic with regards to ADCA exposure. The principal weakness with the Whitehead et al. (1987) study was the harmonization of the statistical measure across the entire exposed

population. In effect, the model used had an underlying assumption that the population was homogeneous when it is known that sensitivity to occupational asthma is not. This resulted in massive levels of variability in their measurements resulting in no detectable dose response.

Similar to Whitehead et al. (1987), the guinea pig study of Gerlach et al. (1989) suffered from assumptions of treatment homogeneity. Standard errors in excess of 50 percent of the respiratory measures were not uncommon in their data set. Fortunately, as part of the post-sensitisation ADCA challenge experiment, the authors indicated that at 50 mg/m^3 exposure, two of the animals showed marked and different responses compared to the other 8 in the treatment group. This could very well be an indication of the population heterogeneity. The probability that the only two sensitive animals would end up in one treatment group is 25 percent: not out of the question. Of course we have no idea how many sensitive individuals may have ended up in the control group either.

The major data gap in both the human and animal studies is the characterisation of the sensitive subpopulation among the exposed population. Without this measure, it is very difficult to determine the potency curves. Mischaracterising individuals who will not manifest sensitisation regardless of exposure results in skewed results and high levels of experimental error.

2.4 Conclusion

Based on the results that are available on the respiratory toxicity of ADCA, it appears that a safe concentration of exposure can be projected to be between 0.5 and 1.5 mg/m^3 time weighted over an 8 hour work day. There are still numerous questions that need to be answered with regard to both the mechanisms of action and population heterogeneity before any statistical certainty can be attributed to these predictions. However, they are well in line with the experience in the UK where 8-hour maximum exposure limits of 1 mg/m^3 in 1996 resulted in a complete halt to reported cases of occupational asthma associated with ADCA exposure.

3. Characterisation of Supply Chain and uses of ADCA

3.1 Introduction

In order to provide an accurate and up-to-date picture of the use of ADCA, a survey of the ADCA Task Force membership was undertaken in summer 2013. Annex 1 provides more detailed information on the survey. The analysis of the results has provided a good understanding of the use, input volumes, processes undertaken, the finished articles in which the substance is used and the size of the market for these products in the EU, although there are thought to be some gaps in response rates, particularly for the U-PVC sector[5].

ADCA is primarily used as a blowing agent in the rubber and plastics industry. It is used in the formulating of mixtures and then as a foaming agent/blend in extrusion, compounding, coating and moulding. Foamed articles produced using the substance are used in a range of downstream sectors such as:

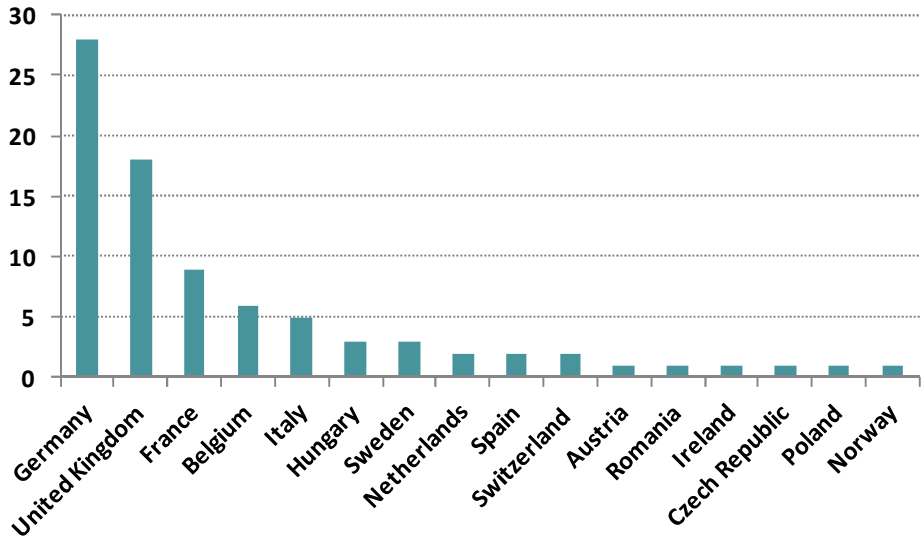
- Rubber: Flexible elastomeric foam (including insulation foam), foamed sheets, cellular rubber profiles, automotive sealants and building products.
- P-PVC: Artificial leather, foamed foils, coated cushion vinyl, wallpaper, flooring and automotive interior surfaces.
- U-PVC: Pipes, foam sheets, roofline and rainwater products.
- Polyolefins: Pipes, cable insulation.

ADCA acts as a blowing agent for processing of the main materials used in each of these applications, and almost all of the substance decomposes in the blowing process.

The figure below shows the geographical distribution of the sites for which data has been analysed in this report. Note that some companies had multiple sites in Europe and multiple sites within the same Member State. From a total of 84 sites, the majority of companies were based in Germany, some 28 or 33%. A further 18 sites (21%) were based in the United Kingdom and 11% in France. Belgium and Italy contained 7% and 6%, respectively, with additional sites in several other Member States.

[5] Information from some of the major suppliers of ADCA (substance/mixtures/compound) to downstream users suggests that, although their downstream users (customers) were contacted and asked to complete the survey, the response rate was low in certain areas, due sometimes to a lack of awareness of the implications of Annex XIV listing. Uses such as U-PVC, which mainly uses formulated ADCA rather than the pure substance are therefore under-represented in the survey results. It is noted that, in a separate survey orchestrated by the British Plastics Federation, U-PVC in cellular applications accounted for 33% of end processors who submitted data (of 21 results not including formulators and distributors for risk of double counting). This would account for a conservative ADCA volume circa 150tonne associated to U-PVC within the UK. The authors highlight that not 'all' users from any individual polymer or sector could be accounted for and the data for UK industry is considered representative but not complete.

Figure 3.1 Geographical coverage of ADCA Survey (location of company site(s))



Note: based on responses from 76 of the 81 responses. Note the data excludes any sites not based in the EU. Some members had multiple sites within the EU and multiple sites within the same Member State. Whilst Norway is not a Member State, the EU REACH regulation has been implemented there.

The remainder of this section outlines the form of ADCA used in Europe. Volumes of ADCA use at various stages of the supply chain are also identified. The functionality of ADCA in the various processes and finished articles is then considered.

3.2 Uses of ADCA

3.2.1 Form of use and volumes

Survey respondents identified the inputs to their business which contained ADCA and the typical ADCA concentration of these. Note, that the concentrations in the final products are significantly lower because the substance decomposes during the polymer processing step. These inputs comprised:

- Pure ADCA powder, with average concentration[6] of 99% w/w, with a range in the result reported between 95% and 100%.
- Mixtures (i.e. pre-blended mixtures of ADCA). These had an average concentration of 49% w/w ADCA. The range of concentrations observed in the results differed substantially (between 3% and 80%).
- ADCA compounds or solid master batches. These had an average ADCA concentration of 29%. Again, the range of concentrations observed in the results differed substantially (between 3% and 80%).

[6] Weighted average based on total quantities of product used across all companies responding.

- Liquid dispersions, paste or non dusting preparations (e.g. oil coated powder). The average ADCA concentration in these inputs was 5%. The range of concentrations observed in the results differed substantially (between 2% and 95%).
- 'Other' inputs account for a relatively small proportion of the total inputs identified. Examples include powder pre-mixes, coated/treated products for processing and inclusion in articles and small volumes of ADCA in samples for testing. The range of concentrations again differed, with a range between 1% and 100%.

The information in Figure 3.2 overleaf presents the results taken from the ADCA survey described above. The information represents ADCA volumes as *inputs* to the various stages/activities described and relate to business activities at EU level. The data does not therefore present product volumes, but ADCA volumes used.

The data is based on inputs from a total of 81 companies (with >80 sites), representing total sales turnover of all products of nearly €28 billion, per year. Of all of the companies combined sales, some 10% (around €2.5 billion) was related to products and processes related to ADCA. It should be noted that a small number of companies involved in the Task Force manufacture large ranges of product types and hence had very large total EU turnovers, only part of which was related to ADCA-based products. For the average Task Force Member, ADCA-related sales comprise 40% of total EU sales; however for many companies, including several of the largest, most or all of their sales are linked to ADCA.

The 81 companies who provided data represent a very good response rate given that the timescales for provision of information were short. The vast majority of companies in the Task Force provided an input and several facilitated inputs from their ADCA-using customers.

Comparing the import volumes of ADCA to the use of the substance in later stages of the supply chain suggests that the survey data covers a significant proportion of the market (in terms of uses)[7]. The total quantity imported is understood to represent the majority of the total ADCA placed on the EU market and the quantity in end uses covered by the survey represents more than half of the quantity imported.

Import Volumes and Distribution

ADCA is not manufactured in the European Union. All ADCA is therefore imported in to the EU[8]. The survey identified a total of some 11,800 tonnes of ADCA which is imported into the EU. Analysis of 2012 trade data for ADCA suggests that total exports of ADCA to the EU,

[7] Note: In instances where volume and substance form data was provided but concentration levels were missing from the questionnaire, an average concentration for all products in that category (i.e. pure ADCA, mixtures, liquid dispersions etc) has been applied.

[8] Under the United Nations Economic Commission for Europe (Recommendation for the transportation of dangerous goods), Part B Classifications. ADCA is listed in Class 4. Division 4.1 (flammable, solids, self reactive substances and solid desensitised explosives. As such, the transportation and storage of ADCA is tightly controlled. ADCA is typically packaged inside a box, with an inner bag, with enforced cello tape to prevent contact from untrained persons. http://www.unece.org/fileadmin/DAM/trans/danger/publi/unrec/rev14/English/02E_Part2.pdf

primarily from Indonesia and China (and to a lesser extent South Korea) suggests that the total imported could be in the order of around 18-19,000t[9].

Whilst it is likely that some firms import small volumes of mixtures containing ADCA and ADCA compounds or master batches, the vast majority, some 95%, is imported in pure powder form. A proportion of the pure powder ADCA is used within companies who both import the product and also carry out subsequent mixing or compounding or processing, but distribution firms covered by the survey receive some 11,500 tonnes of ADCA (though there may be some double-counting here if one distributor supplies to another). The form of ADCA changes little between import and distribution: again, some 95% is pure ADCA powder.

Formulation and Compounding

A total of 18,000 tonnes of ADCA were reported as being used by surveyed companies who develop formulations or masterbatches containing ADCA. The majority of these inputs are in pure powder form (some 89%), but volumes of mixtures, compounds and liquid dispersion / paste each comprise between 550 and 800 tonnes. This total figure includes some double-counting as there are cases where multiple formulation steps occur (i.e. one respondent supplies another formulator) and the total actual amount of ADCA covered does not exceed the 11,800 tonnes above.

A total of some 3,000 tonnes were used in compounding by respondents.

End processors and producers of articles

A total of 11,900 tonnes of ADCA was processed by companies who reported that they undertake end processing activities including production of articles containing ADCA. However, the total amount of ADCA actually used by respondents in processing represents a smaller part of the market, as some companies both (a) undertake production of articles based on ADCA; and (b) supply some of their ADCA to other companies for further processing.

In terms of numbers of companies, the most common use is formulation/blending (some 36% of companies undertake this process); a further 28% undertake compounding. Some 25% undertake extrusion, with 21% carrying out coating, 15% foaming and 4% moulding. Several companies undertake multiple activities and some were indicated as undertaking other (or non-specified) activities.

In terms of quantities of ADCA used in different processing types, moulding accounted for 1% of the quantity used, extrusion 18%, coating 15%, foaming 33% and others 33%.

In terms of finished articles, the largest use of ADCA is in rubber articles, some 5,900 tonnes per year, which is half (50%) of all ADCA volumes used by end processors and producers of articles covered by the survey. End products include:

- Flexible elastomeric foams for thermal insulation in buildings and industrial installations, providing energy savings with low thermal conductivity achieved using low density materials.

[9] Analysis of (partial) trade data suggest that imports from non-EU countries into seven main EU member states were around 17kt in 2012, with the greatest quantities being imported into Germany, Italy, the Netherlands, Spain, Belgium and the UK. However, note that some of the underlying data related to different customs codes and a full analysis has not been undertaken.

- Sealants used in automotive applications to bond metal parts, seal gaps and in construction applications. They seal against dirt/dust and water and prevent corrosion.
- Elastomeric foam used in automotive and domestic seating, table tennis bat coverings, in buoyancy and acoustic (i.e. sound insulation) articles. These foams are also is used to reinforce stiffness of the car body and in crash protection panels.

Based on the estimates of quantities of finished rubber products, the 5,900t of ADCA above could be used in producing over 100,000 tonnes of rubber products per year (the quantity of ADCA used is on average around 5% of the quantity of total finished products, prior to its decomposition).

The average concentration of ADCA in the end product has been estimated and, because of the decomposition of ADCA in the foaming process, the actual concentrations are generally very low. As set out in the 24 June prioritisation document for ADCA, "during processing ADCA is decomposed exothermically to a degree of >99.9% [...] possible remaining ADCA (as well as its non-gaseous decomposition products) are embedded in the polymer matrix and are typically not available".

Some 3,400 tonnes of ADCA are used in polyolefin products, 29% of the total ADCA used in articles covered by the survey. Products include foam rolls, sheets and blocks used in a variety of applications. The corresponding quantity of polyolefin products could be around 200,000 tonnes per year.

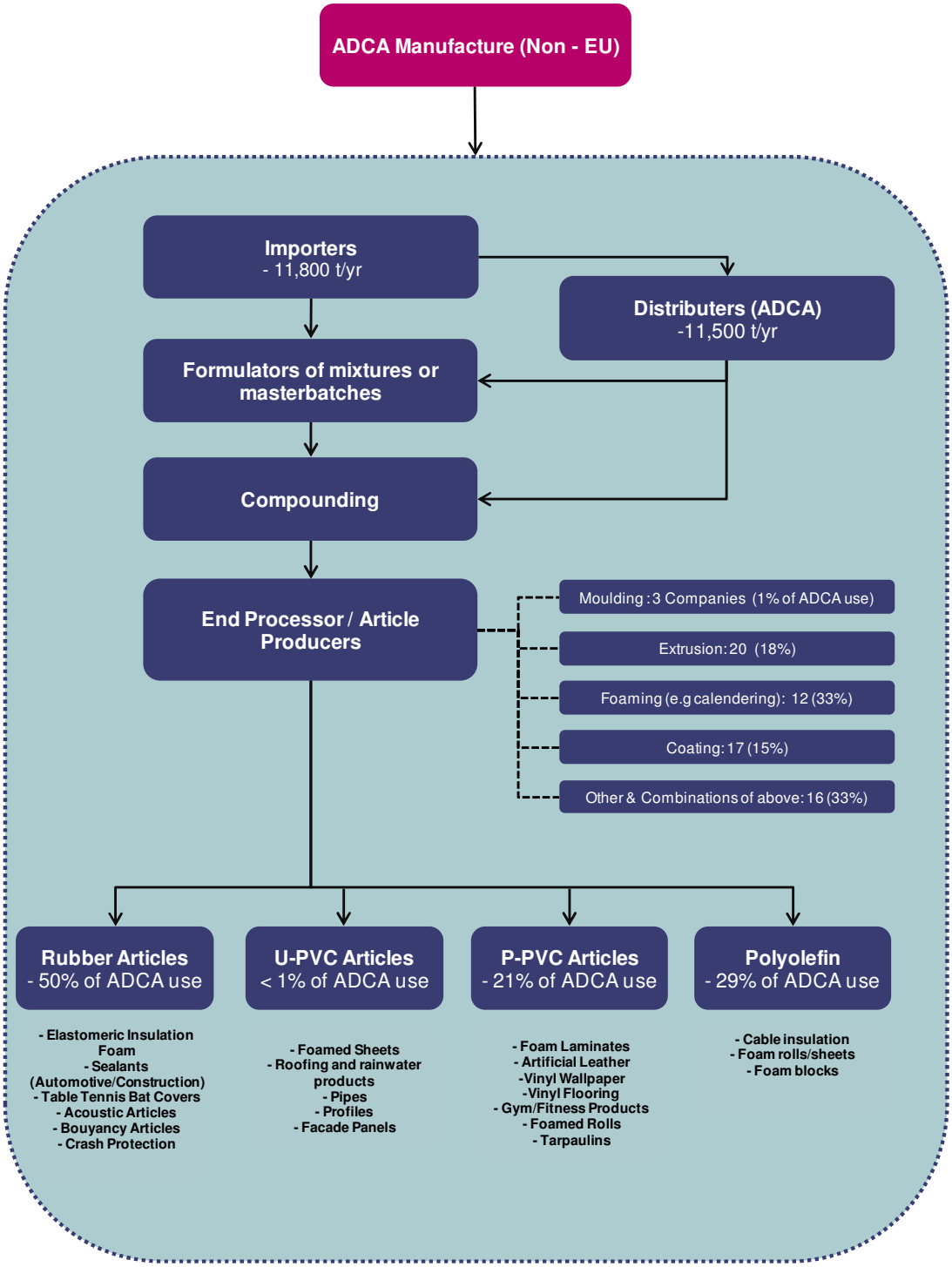
Some 2,500 tonnes of ADCA are used in plasticised polyvinylchloride (P-PVC) articles (21% of all ADCA indentified). End products include foam laminates, artificial leather vinyl wallpaper and flooring, gym/fitness products (such as coated foam matting) and foamed rolls. The corresponding quantity of P-PVC products could be around 250,000 tonnes per year.

Only small quantities of ADCA from amongst the survey responses were reported are used in unplasticised polyvinylchloride (U-PVC) articles: only around 40 tonnes per year has been identified. It is believed that the response rate from this sector was particularly low and anecdotal information suggests that the market size for ADCA in production of U-PVC articles is similar to that for P-PVC. Products include foamed sheets, pipes, profiles and others. This use comprises less than 1% of ADCA use in articles that was identified in the survey.

Overall, the amount of ADCA covered by the survey responses is estimated to cover the majority of EU imports and the majority of EU use of the substance in production of polymers, with each of these comprising around 12,000 tonnes. Total imports may be as much as around 18,000t, suggesting that the coverage is around two thirds of the market. In terms of end users, the most significant gap seems to be in users of ADCA in production of UPVC products, as described previously.

As ADCA is used as a foaming agent to expand the polymer matrix it decomposes in the final processing step. Small traces of ADCA are embedded in the polymer matrix and not released in the form of dust.

Figure 3.2 ADCA Supply Chain



Source: Estimate based on results of survey of ADCA Task Force members (and some customers), summer 2013. Note: Numbers of customers mentioned for processing techniques are those covered by the survey, not total EU estimates.

3.2.2 Benefits of Use

Functionality and benefit in the end product

There are a number of reasons why ADCA is considered, by those responding to the survey, to be advantageous compared to alternative chemical foaming agents[10].

- ADCA is an extremely efficient blowing agent. Its high gas yield enables higher expansion rates in products leading to efficiencies in production through low raw materials and weight saving.[11] The rate of expansion is particularly important in a number of foam based products, such as thermal insulation.
- ADCA contributes to end-product consistency and functionality. The use of ADCA enables fine and consistent cellular structures in a number of polymers, such as polyolefins, U-PVC, P-PVC and rubber products.
  - A consistent cell structure is particularly important in articles such as cable insulation, foam blocks/sheets and rigid PVC products. The cell structure contributes to improved technical performance, and suitable mechanical properties (i.e. not too flexible nor brittle) and longevity of use, in applications such as sound, heat and cellular[12] insulation, in cushioning, shoes soles, gymnasium mats, crash helmets and in sealant products. In certain applicants specific product functionality is required, such water (and water vapour) resistance in pipe insulation, buoyancy (in life jackets) and flexibility (in rolled foam).
  - Uses in insulation products, particularly flexible elastomeric foam, lead to significant energy and space savings compared to alternative materials or products made using alternative blowing agents (see Section 0 for further details).
  - The use of ADCA in vinyl wallpaper supports a '3D' effect or surface texture and contributes to properties such as scratch resistance and 'washability'. Its functionality means additional treatments are not required in certain applications (such as in wallpaper production) saving raw material costs and reducing the weight/ease of use in the final product. Its use in automotive sealant products supports corrosion resistance, prolonging the useful life of mechanical parts.
- ADCA is versatile. Its decomposition properties can be controlled and be adapted to a number of applications. For example, pure ADCA is thermally stable up to around 200°C, but it can be mixed with appropriate "kickers" to perform satisfactorily at a relatively wide temperature range, at least in comparison with alternatives. ADCA can be handled with conventional equipment (e.g. designed for powder handling and compatible with extrusion or injection moulding equipment).

[10] Note that these potential alternatives, their financial and technical feasibility and health, safety and environmental implications associated with their use, is discussed in section five.

[11] 1 g of ADCA yields between 220 and 240 ml/g of gas for expansion. Source: ADCA Annexe XV Dossier. http://www.echa.europa.eu/documents/10162/d9e11c88-481a-47a9-8fff-915b48086ddb

[12] Cellular insulation is a requirement for data cables and coaxial cables with high signal transmission capability, these are used in broadband internet and mobile phone infrastructure.

ADCA does not require specific/unique storage facilities because it is stable in typical environmental conditions.

- ADCA is widely available in sufficient quantities. Its properties support cost effective production processes. It supports running production lines at high speed. The addition of ADCA at relatively small quantities results in overall weight and raw material savings, particularity in PVC applications.

A number of companies have provided information on technical feasibility and cost estimates of the implications of using alternatives. These are discussed in more detail in section five. However, the evidence suggests that, for most uses, no technically feasible alternatives have been identified and that availability of some of the suggested alternatives is limited in any case. In most cases, relatively more of the suggested alternatives, or greater volumes of finished products, would have to be used to achieve the same performance (e.g. insulation). In terms of costs per unit of product performance (e.g. insulation), data suggests that ADCA is competitively priced.

4. Extent of Use and Exposure

4.1 Overview

The suppliers and users of ADCA are of the view that the physical form in which ADCA is used is a key factor affecting the extent to which workers are exposed to the substance. In particular, exposure to ADCA (and related risks of occupational respiratory effects) is only expected to be relevant where ADCA powder is handled and processed. When the substance is used in other forms, such as low dust forms or paste/plastisol, exposure to the dust is expected to be much lower or even negligible. In order to investigate the extent to which companies use different forms of ADCA and related exposure of workers to the substance, the survey undertaken in 2013 attempted to collect information on:

- Number of employees exposed to ADCA in each organisation, according to the type of product used (zero dust, low dust/diluted format, pure ADCA powder, paste and others).
- Number of companies using ADCA in different forms (pure ADCA, mixture (ADCA pre-blended), compound / solid masterbatch, liquid dispersion / paste / non dusting preparation.
- Estimated levels of exposure to ADCA in the workplace, linked to the activities undertaken by the companies concerned.
- Details of risk management measures taken to control exposure.
- Adverse health effects associated with the substance that have been experienced by companies' employees.

The following sections provide details of the results of the survey in terms of the extent of use of different forms of ADCA, followed by a review of levels of workplace exposure and risk management measures in place.

It is believed that the majority of companies handling ADCA powder provided an input to the survey, with users of other forms under-represented (the latter companies often handle much smaller amounts).

It should also be noted that exposure of professionals and consumers is expected to be limited as only industrial uses of the substance are now registered under REACH. While some previous registrations – not the lead registrant's – included some professional and consumer uses, it is understood that these have now been withdrawn or corrected and furthermore that no products for consumer use containing undecomposed ADCA are produced in the EU. Information on ECHA's dissemination website and in the CSRs reviewed for the current study advise against professional and consumer use of ADCA.

4.2 Extent of use of Different Forms of ADCA

The extent of use of a substance, including number of sites, quantities and potential exposure of workers (in this case) are key factors determining the significance of the risks to be addressed by potentially imposing a requirement for authorisation under REACH.

In terms of the numbers of companies using ADCA as an input to their operations in different forms that were covered by the survey, and whether the ADCA was the pure substance or incorporated into a mixture/blend of different forms, it is clear that the majority of companies used the substance as pure ADCA (see Table 4.1). Note however that the ADCA used could be in zero-dust or low-dust form, as considered later.

Table 4.1 Number of companies surveyed that use different forms of ADCA

Process	Pure ADCA	Mixture (ADCA pre-blended)	Compound / solid masterbatch	Liquid dispersion / paste / non dusting preparation	Others	Total
Formulation	23	9	1	5	1	
Compounding	11	4	6	2	1	
Moulding	0	3	0	0	0	
Extrusion	10	2	8	4	1	
Coating	8	1	0	4	3	
Foaming (e.g. calendering)	8	4	0	4	0	
Other	3	3	1	5	1	
Sum of above	63	26	16	24	7	
Actual total	48	22	13	22	7	112
% of total	43%	20%	12%	20%	6%	100%

Note: The "actual total" number of companies using each type is less than the sum of the individual rows/columns because some companies use two or more forms. The total number of companies covered was 77, so the figures in the "actual total" row indicate that several companies also undertake more than one activity.

The total quantity of ADCA handled by Task Force companies indicated as formulating the substance is around 11,800 tonnes, which is estimated to cover almost all of the ADCA used in the EU (unless any major importers have not been identified). However, the quantity indicated as being used by companies undertaking each of the polymer processing activities is thought to only represents around two thirds of the total used in the EU.

In order to estimate total number of companies using different forms of the substance, the numbers undertaking the polymer processing activities were extrapolated using the above tonnage figures, to give the estimates below for total number of companies using each of the

different forms. It is noted that these could be an underestimate, for example if mainly companies using larger quantities are represented in the survey respondents. However, as stated earlier, the survey responses are believed to have covered the majority of use of ADCA powder, with use of other forms (e.g. liquid dispersions, pastes) under-represented, meaning that the overall percentages of use of pure ADCA at EU level may well be lower.

Table 4.2 Estimated number of companies in EU that use different forms of ADCA

Process	Pure ADCA	Mixture (ADCA pre-blended)	Compound / solid masterbatch	Liquid dispersion / paste / non dusting preparation	Others	Total
Number	65	30	19	34	11	159
% of total	41%	19%	11%	21%	7%	100%

Note: Number of companies was based on data from survey respondents (Table 4.1) with numbers of formulators not adjusted, but numbers undertaking each processing activity extrapolated based on the % of the total ADCA use covered by the survey that is estimated to be covered by the end-users amongst the survey respondents. Numbers of companies undertaking compounding were not adjusted.

Note again that the total number in the above column includes some companies which use more than one form of the substance.

The number of employees exposed to different forms of the substance is of great importance with regard to the potential for adverse health effects. In a number of the activities highlighted in the 'draft background document' for ADCA as likely to be associated with the highest potential for inhalation exposure, it is important to note that the activities will often not involve exposure to ADCA dust (e.g. calendering, PROC 6) will often involve use of the substance as part of a paste/plastisol, where there is negligible potential for exposure to the dust, except where ADCA powder is used as an input to this process.

Survey respondents were asked to estimate the number of employees in their organisation exposed to different forms of the substance, particularly whether the use relates to the pure powder, or to low/zero dust forms, or pastes/liquid. Table 4.3 provides details of the survey responses (responses to this question were received for 71 of the 81 companies that responded to the survey).

Table 4.3 Estimated number of employees exposed to different forms of ADCA from survey

Process	Zero dust	Low dust/diluted	Pure ADCA powder	Paste	Other	Total
Formulation	107	71	227	393	62	
Compounding	735	115	136	79	21	
Moulding	0	0	6	0	150	
Extrusion	599	173	107	115	34	
Coating	194	28	38	823	35	
Foaming	15	82	124	20	12	
Other	24	9	26	50	40	
Sum of above	1674	478	664	1480	354	
Actual total	1228	371	525	1080	297	3501
% of total	35%	11%	15%	31%	8%	100%

Note: The actual total number of employees exposed is less than the sum of the individual rows/columns because some employees undertake two or more processes (or use two or more forms)

It is noted that the draft background document on the prioritisation of ADCA referred to a number of polymer processing activities[13] as likely to be associated with the highest potential for inhalation exposure levels in comparison to other processes. It should be noted that the updated REACH registrations do not include e.g. PROC 7 for industrial spraying and brush coating is not relevant (and no information on these uses has been identified in the survey). Furthermore, for calendering (foaming) operations, while some companies undertaking this process use ADCA powder, it is more often used in e.g. paste form, without the same potential for exposure to ADCA powder.

Again, these data were extrapolated to give the potential number of employees exposed to different forms, based on the fact that only a proportion of the total ADCA use is accounted for in the survey responses for the different polymer processing activities. This information is contained in Table 4.4.

[13] For example calendering operations (PROC 6), industrial spraying (PROC 7) and roller application or brushing (PROC 10).

Table 4.4 Estimated number of employees exposed to different forms of ADCA in EU

Process	Zero dust	Low dust/diluted	Pure ADCA powder	Paste	Other	Total
Number	1697	546	708	1645	472	
% of total	34%	11%	14%	32%	9%	100%

Note: Number of employees was based on data from survey respondents (Table 4.3) with numbers undertaking formulation not adjusted, but numbers undertaking each processing activity extrapolated based on the % of the total ADCA use covered by the survey that is estimated to be covered by the end-users amongst the survey respondents. Numbers of employees undertaking compounding were not adjusted. Note that the total number of employees using ADCA is less than the total above because some employees will use more than one form of ADCA.

Based on the above, whilst the number of companies handling ADCA is likely to be in the order of hundreds, the number of companies handling pure ADCA is more likely to be in the region of several tens of companies.

Likewise, whilst the number of employees using ADCA or ADCA-based products is likely to be several thousand, the number of employees exposed to pure ADCA powder (assumed to have the greatest potential for inhalation exposure) is likely to be a small part of this, probably in the order of several hundred.

Note that the above estimates for total numbers at EU level are considered to be more accurate for employees than for companies, as the number of employees is more likely to be correlated with the quantity of ADCA used. Numbers of companies are considered less reliable and potentially an underestimate because it is possible that many smaller companies using small quantities of the substance would not have participated in the survey.

4.3 Workplace Exposure

The survey undertaken attempted to collect information on the levels of measured exposure to ADCA in the workplace, in the form of workplace concentrations. Only a relatively small number of companies were able to provide estimates of workplace concentrations, as data were not available in many cases (at least within the timescale for collection of information, in August 2013).

The data that were provided allow estimates to be derived of the different exposure levels measured and these have been correlated with the numbers of employees exposed at each of these companies. However, it should be noted that the data reported are based on a variety of different averaging periods, taken from a variety of different locations within the workplace (some typical and some worst case) and the parameters measured varied significantly (in some cases being only total dust).

Figure 4.1 provides details of the different measured concentrations for companies using pure ADCA powder and for all other forms combined (each as a separate line). It shows the percentage of employees in workplaces where concentrations were measured at different concentration levels from the responses provided.

Figure 4.1 Numbers of workers in facilities with measured concentrations below different concentration levels

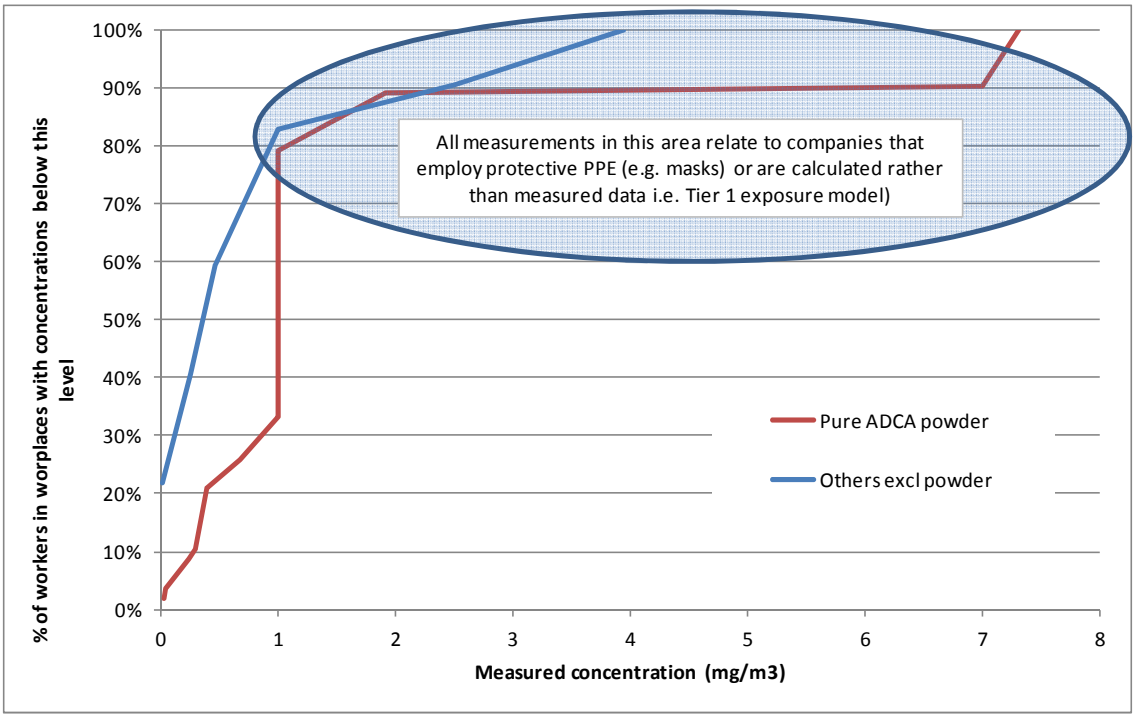


Figure notes: Exposure levels included are typically up to 8h TWA values rather than short term, although some data are understood to relate to short-term exposure only. It should be noted that many companies did not provide measured data on exposure levels, either because they were not available within the timeframe of this study, or because they employ protective equipment such as masks to limit exposure of workers (sample size was 13 companies and 163 workers for pure ADCA; 6 companies and 64 workers for other forms). The figures provided only include those where quantitative estimates were given in the survey. As highlighted in the figure, some of the figures provided included only total dust estimates, which have been corrected for ADCA content where possible, but not in all cases. Furthermore, some of the data provided are based on maximum values (i.e. result was given as <X mg/m3). Levels above 1mg/m3 for 'others' relate only to compounding and relate to 'low-dust' format, rather than dust free or to estimates believed to be modelled rather than measured. Some figures were normalised for an 8h shift based on worst case measurements over a shorter period.

The data indicates that workplace concentrations of ADCA are generally higher (and more employees are potentially exposed to higher levels) where pure ADCA powder is used. The majority of workplaces where measurements were available (expressed through number of employees) had concentrations below relevant limit values such as the UK's STEL of 3 mg/m3 and 8h-TWA of 1 mg/m3. Nonetheless, there was a relatively small number of respondents who reported concentrations in excess of these values, although some of these values were older, historical measurements and often related to total dust, rather than just ADCA. Furthermore, the risk management measures specified in the ES/eSDS for the substance would mean that actual employee exposure would be significantly lower (e.g. a mask as specified in the safety data sheet would protect against concentrations in the workplace), particularly given that workplace concentrations are understood to have reduced significantly over recent years.

There are a number of important provisos to take into account in relation to the above data, including:

- Some of the highest concentrations measured are historical values, measured before the introduction of more stringent risk management measures.
- The workplace concentrations levels are likely to be an overestimate of actual average concentrations, because in many cases only maximum measured concentrations were provided by companies. In a small number of cases only modelled exposure levels (using tier 1 exposure models) could be provided. Furthermore, in some cases, the data provided related to total dust, rather than either ADCA itself or respirable dust.
- The workplace concentrations are not necessarily indicative of levels to which workers will actually be exposed: In most cases additional risk management measures are applied, as discussed in the next section.
- In many cases, data were not provided on the averaging period used for the exposure measurements (e.g. short-term or long-term). For convenience, and in the absence of better data, all data have been treated equally in the above figures. (Some companies had measured data over 15 minutes, up to 8 hours, and various timescales between these values.)
- It was noted by many companies that workers would only be exposed to these maximum levels for short periods of time during a typical shift, rather than being exposed over the course of a whole shift.
- A number of companies reported 'zero' concentrations in the workplace, meaning that the numbers below each concentration level will actually be higher than those in the figure above.

4.4 Risk Management Measures

Since ADCA is acknowledged in law to be a respiratory sensitiser, the majority of companies are expected to have in place risk management measures to limit exposure of workers.

The REACH registration information for ADCA, based on ECHA's dissemination website, includes the following in terms of specified exposure controls / personal protection (selected measures only):

- Information for safe handling:
  - Prevent formation of dust.
  - Use appropriate industrial vacuum cleaners or central vacuum systems for dust removal.
  - Ensure good ventilation/exhaustion at the workplace.
- Exposure controls / personal protective equipment:
  - General protective and hygienic measures: during processing, ensure efficient ventilation in the working area.
  - Respiratory protection: dust mask; good ventilation is desirable and respiratory protection during dust formation; in case of brief exposure or low pollution use

respiratory filter device; in case of intensive or longer exposure, use self-contained respiratory protective device.

- Protection of hands: protective gloves (impermeable and resistant); use of skin-protecting agents is recommended.
- Eye protection: safety glasses.

Whilst these measures are set out in the registration information, it is possible that some of the downstream users of the substance do not have access to all of this information via the CSR or eSDS (in particular for mixtures, where the deadline is 2015 for the requirement to supply a REACH eSDS). It is therefore possible that uptake of risk management measures will further improve over time, as users become more aware of the measures required to ensure safe use communicated through the supply chain.

In order to better understand the actual exposure of workers involved in processes using ADCA, survey respondents were asked to provide information on the risk management measures applied at their facilities. Table 4.5 provides a summary of the number of companies applying each of a range of exposure controls and protective equipment.

Table 4.5 Risk management measures applied by survey respondents

	% of all companies responding	% of companies that handle ADCA powder
Mask	73%	81%
Mask or "PPE" unspecified	80%	86%
Gloves	39%	45%
Goggles	18%	19%
LEV/extraction	73%	79%
Closed system	18%	17%
Liquid/zero dust formulated ADCA as RMM	8%	0%
One or more most relevant controls (mask / PPE / LEV / closed system / zero dust)	100%	100%

Based on inputs from 66 of the total 81 companies that responded to the survey (companies that did not respond were excluded from the data). Several companies apply more than one of the risk management measures.

From the above, it can be seen that all of the companies responding apply at least one of the more important risk management measures that will protect workers against exposure to the dust, such as use of masks, closed systems and local exhaust ventilation / extraction. A significant number apply each of these risk management measures and many companies apply several of them. The application of such risk management measures will mean that actual concentrations that workers are exposed to will be significantly lower than the measured concentrations in the workplace discussed in the previous section.

4.5 Past Cases of Adverse Effects

As part of the survey, companies were asked to provide details of any cases of adverse effects experienced by their employees that may be directly or indirectly attributed to ADCA exposure, including the timescales over which this occurred. Key results are summarised in the table below.

Table 4.6 Responses from companies on adverse health effects

	No of companies	Notes
No cases reported	47	
No cases in last 10 years	1	Case was reported as not clearly linked to ADCA
No cases in last 11-20 years	6	One case reported as not clearly linked to ADCA. Not all companies had any actual cases – some reported e.g. "none in the last XX years" but this does not mean that there were any cases before this.
None in last 21+ years	2	No cases
Total companies responding	56	

Based on the above (and analysis of the underlying information), the following conclusions can be drawn:

- No cases were reported in the vast majority of companies.
- One company reported a case in the last 10 years, although this was not clearly linked to ADCA.
- A few noted that there were none in the last 11-20 years, but this includes some who only reported on 11-20 years of operation (i.e. because their business started within those timescales, they reported e.g. 'none in the last 15 years'). In these cases, they effectively have not had any reported cases.
- Of all of the companies that responded, the number who have actually reported any cases is <5 over the last 20 years.
- Companies that reported having historical health impacts indicated that no problems had been encountered since extraction (local exhaust ventilation) and/or masks have been introduced.

No information has been identified suggesting any adverse health impacts for consumers (or indeed workers) associated with exposure to finished products available to the public, such as articles or any other plastic materials. This is unsurprising given that almost all of the ADCA decomposes during the foam blowing process, leaving only small amounts in consumer products, which itself is not readily released from the polymer matrix.

5. Socio-economic Importance and Implications of (non) Authorisation

5.1 Implications of Refused Authorisation

The survey collected information to better understand the expected response of companies at various stages of the supply chain to a possible restriction on ADCA and the resultant economic and other implications for them and their customers. Specifically, information was sought (on a confidential basis) from companies on:

- The likely response of companies to a restriction on ADCA, along with views on the resultant response by further downstream users including final consumers.
- Information on the implications of no longer being able to use the substance in terms of economic/commercial effects; performance and technical issues; health, safety and environmental risks; social impacts; and wider economic impacts.

These implications are clearly linked to companies' views on the suitability and availability of alternatives, which is covered in section 5.4.

The information collected provides a useful indication of the potential socio-economic implications of a requirement for authorisation. More detailed information would be required for an authorisation application in the event that ADCA is ultimately included on Annex XIV.

5.2 Expected Response Scenarios

This section provides an overview of the likely response to a restriction of the main actors involved in the industry. It is important to note that many companies fell into multiple supply chain categories. The response scenarios vary depending on various factors, such as the proportion of turnover from affected product lines relative to overall turnover; the presence of existing non EU sites that would facilitate relocation; the stage(s) in the supply chain and the degree to which companies' judge the investment in alternatives is practicable and worthwhile.

Notwithstanding these issues, overall there were consistent messages amongst the respondents regarding what companies' responses would be to no longer being able to use ADCA, specifically:

- For importers and distributors[14], companies would either cease trading within the product lines concerned (which in some cases is expected to result in closure of the business entirely) or would relocate that part of the business to outside the EU so that they can still supply non-EU markets. In some cases existing non-EU sites would facilitate this relocation, for others this is likely to involve substantial costs and job losses.

[14] Note, many companies are involved in numerous process stages. For the purposes of this analysis, companies are classified according to their 'first' role in the supply chain (i.e. an importer and article producer is classified as an importer).

- For formulators and compounders there was greater uncertainty over the possible response scenarios, reflected in a diversity of responses. These can be grouped into four broad categories.

    - First, a number of companies would consider producing and/or using alternative substances, subject to feasibility testing and transitional costs. In several cases this was expected to have adverse effects, particularly on article weight and raw material volumes and costs. This is not a straightforward issue and is likely to be a very costly and time-consuming process. For some product types, substitution would be possible but product quality and performance would reportedly be different and/or inferior, leading to implications for consumer acceptability. This may lead to a loss of (part of) the relevant market, due to reduced demand for these new ADCA-free products. For some products, efforts to reformulate might lead companies to conclude that adequate product performance cannot be achieved with potential alternative substances and the entire product line would be terminated without their ability to use ADCA as an ingredient. In this case, there would be a total loss of the relevant market.

    - Second, several companies would expect to relocate outside of the EU. For some companies, but not all, the expectation is that such a relocation would mean they effectively 'abandon' their business in a particular sector/product area consolidating into a smaller number of product lines, given particular expertise and/or process/production facilities currently within the EU.

    - Third, some companies do not expect to relocate outside of the EU, but expect sales to be adversely effected or to abandon a market area or sector, with associated loss of turnover and redundancies.

    - Fourth, a small number of companies considered business closure would be a realistic outcome.

A similar range of responses were provided by firms who are end-processors or producers of final articles. A small number of companies considered that they would use alternative products where feasible, although several companies would expect to relocate outside of the EU, where it would presumably still be possible to use ADCA in producing foamed articles. As above, a small number of companies expected business closure would result.

It should be noted that the most common response was that imports of certain products from outside the EU would increase, because foamed-articles could still be produced outside the EU and imported, even if authorisation is not granted in the EU. Given the significant use of ADCA in various stages/processes in the supply chain, any significant increase in non EU imports are likely to have socio-economic implications along the entire supply chain, potentially resulting in additional business closures.

There were no clear patterns amongst product types: all are expected to be affected by an increase in imports; however a number of consultees mentioned the relative ease with which end users could use non-EU-manufactured foam products. Moreover any significant switch to non-EU imports would prevent the necessary investment in potential alternatives because the market would be in effect decreasing in size.

Whilst groups representing consumers of products that have been produced using ADCA were not consulted as part of the survey, the task force members provided information on the likely response of consumers and any (further) downstream users to a loss of the substance.

In this context, a common response was that end prices were expected to increase, resulting from a loss of production efficiency and the relative costs of ADCA compared to potential alternatives, noted above. Transportation costs for some bulky foam applications are typically high (due to the low density), which may also impact prices paid by the end user. Small numbers of companies indicated they expected consumers to use alternative products (in at least in some circumstances these are also likely to be imported from outside the EU). In some specialist applications, companies considered that consumer choice would be adversely affected.

5.3 Socio-economic Implications

5.3.1 Lost turnover and business closures

Table 5.1 provides information on the annual turnover generated within responding companies from the sale of ADCA-related products; this information relates to activities within the EU only. Overall, the 77 companies derive just over €2 billion from ADCA-related activities. On average, these activities generate some €35 million turnover across Europe, per year, in each firm[15]. The majority of this turnover is generated by the more numerous formulation and compounding firms amongst the responders (some €1.3 billion) and by end processors and article producers (some €700 million). For the EU as a whole, the value for end-processors will be substantially higher, as many downstream user companies (e.g. small article producers) could not have responded to the survey, given the limited time available.

The proportion of total company turnover generated by ADCA product lines is also shown. Overall, companies that import and/or distribute the product generate around a third of their total turnover through ADCA[16]. For formulators and compounders, the figure is somewhat higher – just under 40%, whilst for end processors, ADCA-related products account for almost half of all turnover (47%). This suggests that, in the event that ADCA was subject to a refused (or not-applied-for) authorisation under REACH, a substantial proportion of the companies that took part in the consultation would be significantly affected, unless technically and economically feasible alternatives could be used.

[15] Note this relates to total turnover related to ADCA use.

[16] Note that this category includes a number of firms who also carry out downstream formulations and in some cases also manufacture articles/end products.

Table 5.1 Value of ADCA product lines as a proportion of total annual turnover

	Total turnover (ADCA product lines)	Average proportion of total Company turnover generated by ADCA product lines
Importers and Distributors	€120,000,000	34%
Formulation of mixtures/masterbatches containing the substance and compounding of ADCA	€1,300,000,000	39%
End processor / producer of articles using ADCA	€700,000,000	47%
Other	Conf	~

Based on inputs from 67 of the total 77 companies that responded to the survey. The estimates only cover companies responding to the survey and total turnover in the EU will be higher. Numbers have been rounded. Note that there were at least ten firms in each category where data has been reported. The percentages shown are averages of all firms in each category. Many firms carry out activities win a number of categories and were classified according to the 'first' activity' undertaken (e.g. importing). Those classified as 'other' are potentially disclosive and are not presented.

5.3.2 Other Costs

Substantial costs are expected to be incurred through the loss of capital value of production plant which - based on annual turnover values and operational lifetime of the equipment involved - are likely to be significant.

Research and development (R&D) costs would be incurred for any substantial reformulation or adoption of alterative substance. Substantial plant/equipment investment; product approval; testing; and marketing costs would also be incurred. Where costs have been identified, these are expected to amount to tens of millions of Euro.

In certain applications, it is anticipated that some manufacturing processes would have to be run at slower speeds if alternatives are used, leading to lost turnover/productivity. Potential alternative substances are examined below, however the evidence suggests that it is not clear that technically and economically feasible alternatives exist for almost all of the applications. The evidence provided by Task Force Member suggests there are considered to be no suitable alternatives in many of the applications, suggesting that turnover from these applications will be lost to the EU.

Where alternatives are potentially feasible (albeit with inferior product performance), different equipment is likely to be required alongside additional safety measures where the alternatives are explosive and / or flammable, such as isopentane, OBSH and DNPT.

5.3.3 Employment

A total of 20,000 employees have been identified amongst firms which provided information in the survey[17]. Any loss of the market for EU products that could not be replaced by alternatives would have implications for employment. Hypothetically, if 100% of current sales of ADCA-

[17] Based on inputs from 69 of the total 81 companies that responded to the survey.

using products were lost, it is tentatively estimated that the number of EU jobs lost amongst Task Force members could be up to the order of some 17,000[18].

Table 5.2 Employment numbers within survey respondents (mainly Task Force members)

	Total Employees within the organisation (EU based only)	Hypothetical effect if 100% of ADCA sales are lost
Importers and Distributors	500	c.200
Formulation of mixtures/masterbatches containing the substance and compounding of ADCA	12,500	c.5,000
End processor / producer of articles using ADCA	4,200	c.2,000
Other	Conf.	~
Total	17,200	c.7,200

The survey respondents include a high proportion of companies towards the top of the supply chain, each of which will handle relatively large quantities of ADCA. Amongst the end-users (plastics and rubber product manufacturers/converters), the amounts of ADCA used per company will be relatively smaller given that these companies will often use dilute forms such as plastisols (though the amounts of end products produced will be high). This means that the end-users will have many more employees per tonne of ADCA used. It is thought that the number of employees involved in ADCA-related plastics and rubber processing activities is in the order of a few hundred thousand people, with the number of 'indirect' jobs greater still.

5.3.4 Wider economic impacts

The main wider economic impacts of a potential refused authorisation are likely to relate to international trade and the competitiveness of the EU. In the event that ADCA is restricted in the EU and not in other parts of the world, it is likely that demand for ADCA-containing products would remain outside the EU and non EU companies would retain the cost efficiency benefits that the use of ADCA brings, potentially affecting the end prices paid by consumers.

Non-EU companies would still be able to use ADCA and supply the articles that they produce to the EU market, thus representing a reduction in the competitiveness of the EU.

5.3.5 Health and Environmental Impacts

A potential refused authorisation is expected to result in adverse environmental impacts, in at least some applications. These are expected to arise from three sources. First, as noted above it is considered likely that non-EU imports of a number of articles, in particular elastomeric foam would increase, with the associated greenhouse gas emission arising from their transportation and distribution. Second, the high gas yield of ADCA and its closed cell structure mean it is an efficient insulation material, contributing to energy efficiency in buildings and other

[18] Note this is based on applying the proportion of total turnover to the employment numbers identified. It includes only those companies which provided data on both employment numbers, total turnover and turnover generated through ADCA product lines.

applications. Even in cases where alternatives could be used, a thicker insulation material is unlikely to be acceptable in at least some instances, including significant end uses such as in cavity wall insulation in housing. Third, in the event ADCA could no longer be used it is anticipated that, in those applications where alternatives might be introduced, greater quantities of the alternative substances would be required. This would result in an associated increase in emissions associated with transportation and distribution.

The implications of alternatives are examined below. The evidence suggests additional employee safety risks and/or ecotoxicological risks could be introduced through their use which would offset any health benefits associated with reduced use of ADCA. (No attempt is made here to comment on the likely net change in health/environmental harm.)

5.4 Implications of Alternatives

Information has already been considered (in the prioritisation of ADCA for the candidate list) on a number of substances suggested as alternatives by raw material suppliers, including some information on health, safety and environmental implications of those substances. Table 5.3 overleaf evaluates the potential alternatives that are mentioned in publicly available documents published by ECHA and desk-based research on its commercial availability. Where the survey responses provided consistent messages on the suitability of alternatives, these are also included (other data were considered confidential and are not included in this note).

The categories in the table are taken from ECHA's guidance document on the preparation of authorisations for application, particularly section 3 (analysis of alternatives)[19].

Overall, whilst the majority of respondents acknowledge there may be some, limited applications where substitution may be possible, albeit with some loss of product functionality/quality, the consensus amongst those consulted was that there is no technically suitable alternative to ADCA without an unacceptable loss of functionality/quality or global competitiveness. Concerns were also expressed that the use of alternatives could potentially introduce risks arising from substances that are less thoroughly tested through the (eco)toxicological impacts that they may pose, as well as through inferior product performance.

[19] http://www.echa.europa.eu/documents/10162/13637/authorisation_application_en.pdf.

Table 5.3 Information on alternatives based on ADCA Task Force responses

Substance	Public document where it is identified as a potential alternative to ADCA	Technical feasibility	Economic feasibility	Applications mentioned / tested	Environment and human health hazards and risks	Availability
Key Question for the analysis [Note 1]		*Can the alternative fulfil or replace the function of ADCA?*	*What are the changes in costs and revenues including possible pass-through of cost to customers of transferring to an alternative substance or technique?*	*In which application(s) have these alternatives been suggested as possible alternatives and/or tested by Task Force members?*	*Does the alternative represent a reduction in overall risk compared to ADCA, taking into account risk management measures and operational conditions?*	*What are the timescales that may be required to make possible alternatives suitable and available for the applicant, taking into account relevant R&D where appropriate?*
4,4' Oxy di-(Benzenesulfono hydrazide) (OBSH)	Annex XV Dossier [Note 3]	Potential to substitute in some applications. Significantly less efficient (i.e. the volume required is expected to double). Substance has a lower gas yield than ADCA, greater quantities are required in generation of foams with low densities. For insulation materials its use is reported to result in higher material density and higher thermal conductivity. Where used for insulation, significantly greater quantities of the material would be required (i.e. thicker insulation). Decomposes at a lower temperature than ADCA. The actual decomposition temperature in combination with a lower process speed (to ensure complete decomposition) can damage foam products (a burning/darkening of the foam surface). The temperate at which they decompose would make them unsuitable for the processing of many polymers. Its use is restricted to low temperature applications and this would prevent use in the processing of many	The greater quantities of material required would occupy increased processing / production and storage space and is expected to result in higher prices for the end consumer. Substantial investment at plant where it is used in place of ADCA due to safety issues (see right). Higher costs of production. It is considered to be three to four times more expensive than ADCA.	Vinyl wallpaper (but additional costs, and health/safety implications). Rigid PVC (but significant additional costs). Rubber/EPDM sealants (but loss of product functionality). Flexible elastomeric foams (but environmental implications due to reduced quality of product and additional costs). Certain applications of cross linked polyolefin foams (but negative environmental and technical implications).	Explosive. Dangerous for handling and processing. Limited data available. Relevant Classifications [Notified classification and labelling health and environmental hazards]: H302 Harmful if swallowed H315 Causes Skin irritation. H319 Causes serious eye irritation H334 may cause allergy or asthma symptoms or breathing difficulties if inhaled H335 May cause respiratory irritation. H341 Suspected of causing genetic defects H350 May cause cancer (note	Commercially available [Note 2] but limited availability. OBSH was registered under REACH in 2013. No EU producer. Responses to consultation on timescales for use of possible alternatives vary and are subject to the information presented left. The information is not reported by substance but timescales are anticipated to be between 3 and 10 years. It has not been possible for the consultees to

Substance	Public document where it is identified as a potential alternative to ADCA	Technical feasibility	Economic feasibility	Applications mentioned / tested	Environment and human health hazards and risks	Availability
		applications. Foam expansion when using OBSH was difficult for operators to control to ensure appropriate thickness and mechanical properties.			this has been notified by a small number of companies only) H411 Toxic to aquatic life with long lasting effects	estimate with accuracy, but costs are likely be substantial, with ranges of between €40,000 to up to €1,500,000 per product with overall costs per firm of several million reported. For some the costs of reformulation are prohibitive and may lead to firm closure.
Sodium Bicarbonate	Annex XV Dossier[Note 3]	Significantly less efficient (i.e. the volume required is expected to double). Cannot be used alone for PVC application, (it has too coarse a cell structure and its decomposition temperature is not consistent with the process temperature ranges required). It is used alongside ADCA. In at least some applications (flooring, wallpaper, artificial leather) specifications cannot be met. Water absorption is a problem. Not typically used alone but in mixtures/batch. It is not considered suitable for the majority of rubber foams, not suitable for thermal insulation flexible elastomeric foam (FEF). Products containing sodium bicarbonate absorb water, this has a negative impact on the foaming properties of the product; the bicarbonate can partially deactivate or be washed out.	A low cost foaming agent compared to ADCA. However this is offset where used for insulation, as significantly greater quantities of the material would be required (i.e. thicker insulation). The greater quantities of material required will occupy increased processing / production and storage space and is expected to result in higher prices for the end consumer. The deactivation noted (see left) has an adverse effect on product shelf life and requires shorter production runs, which results in higher production costs.	Foamed cushioned vinyl wall-covering (but loss of product functionality and additional costs). Some low expansion block foams (but implications for product functionality/quality).	None identified. Not classified in ECHA C and L Inventory.	Commercially available.

Substance	Public document where it is identified as a potential alternative to ADCA	Technical feasibility	Economic feasibility	Applications mentioned / tested	Environment and human health hazards and risks	Availability
Isopentane	Comments on Annex XV Dossier for identification a substance as an SVHC and response to those comments (ADCA). [Note 4]	Expected to result in significantly inferior product quality of foamed products (e.g. consistency), in at least some applications. For insulation materials its use is predicted to result in higher material density and higher thermal conductivity. Where used for insulation, significantly greater quantities of the material would be required (i.e. thicker insulation). It is therefore not considered a suitable alternative for flexible elastomeric foam.	The greater quantities of material required would occupy increased processing / production and storage space (different processing equipment would be required) and is expected to result in higher prices for the end consumer. Expected to result in shorter lifetime of end products.	Foaming, but use is limited to high pressure foam extrusion equipment, with differing cell structures and so not suitable for many products where ADCA is used.	Substance is flammable, hence potential safety issue [Note 5] Relevant Classifications [No notified classification and labelling under health and environmental hazards].	Commercially available.
Isobutane	Comments on Annex XV Dossier for identification a substance as an SVHC and response to those comments (ADCA). [Note 4]	Isobutane-foamed materials contain larger cell sizes, which leads to reduced thermal insulation. The foam exhibits uneven thickness and is expected to result in significantly inferior product quality of foamed products (e.g. consistency), in at least some applications. For insulation materials its use is predicted to result in higher material density and higher thermal conductivity. Where used for insulation, significantly greater quantities of the material would be required (i.e. thicker insulation). It is therefore not considered a suitable alternative for flexible elastomeric foam.	The greater quantities of material required will occupy increased processing / production and storage space (different processing equipment would be required) and is expected to result in higher prices for the end consumer.	Foaming, but use is limited to high pressure foam extrusion equipment, with differing cell structures and so not suitable for many products where ADCA is used.	Substance is flammable hence potential safety issue [Note 6]. Relevant Classifications [No notified classification and labelling under health and environmental hazards]	Commercially available.
Toluene sulfonyl hydrazide (TSH)	Comments on Annex XV Dossier for identification a substance as an SVHC and response to those comments (ADCA). [Note 4]	Decomposes at temperatures below the suitable processing temperatures of many polymers and can disable the foaming action. Their use is restricted to low temperature applications, preventing use in the processing of many applications. Foaming action would be difficult to control and adversely affect quality/consistency of cushioning, thermal insulation and decorative structure (i.e. wallpaper). TSH is not feasible for thermal insulation foam	Reduction in efficiency (hence requiring greater volumes). Unit cost for TSH is greater than ADCA.	Vinyl wall-covering (but additional costs). Rubber/EPDM sealants (but loss of product functionality). Some closed cell rubber applications (but some loss of functionality and potential loss of consumer acceptability).	Limited data available. Substance Is flammable. Relevant Classifications [Notified classification and labelling health and environmental hazards]: H301: Toxic if swallowed H315: Causes skin irritation H319: Causes serious eye	Commercially available [Note 7]. but limited availability. No EU producer.

Substance	Public document where it is identified as a potential alternative to ADCA	Technical feasibility	Economic feasibility	Applications mentioned / tested	Environment and human health hazards and risks	Availability
		because the decomposition temperate is too low for NBR and EPDM rubber.			irritation H334 may cause allergy or asthma symptoms or breathing difficulties if inhaled H411 Toxic to aquatic life with long lasting effects	
P-Toluene sulfonly-semicarbazide (TSSC)/ Also referred to as PTSS.	Comments on Annex XV Dossier for identification a substance as an SVHC and response to those comments (ADCA). [Note 4]	Significantly less efficient (i.e. the volume required is expected to double). For insulation materials its use is predicted to result in higher material density and higher thermal conductivity. Where used for insulation, significantly greater quantities of the material would be required (i.e. thicker insulation). Adverse effect on product quality of foamed products, in at least some applications.	The greater quantities of material required would occupy increased processing / production and storage space and is expected to result in higher prices for the end consumer. It is considered to be between five and up to ten times more expensive than ADCA.	Certain applications of cross linked PP foams (but environmental and technical implications)	Limited data available. Relevant Classifications [Notified classification and labelling health and environmental hazards]: H302 Harmful if swallowed H312 Harmful in contact with skin H319 Causes serious eye irritation H332 Harmful if inhaled. H335 May cause respiratory irritation.	Commercially available. Does not appear to be manufactured in the EU[Note 8].
5-Phenyltetrazole (5PT)	Comments on Annex XV Dossier for identification a substance as an SVHC and response to those comments (ADCA). [Note 4]	Its decomposition temperature (270ºC) is too high for many ADCA applications. Significantly less efficient (i.e. the volume required is expected to increase by around a third). Generally limited use in Europe due to the small process window and low levels of gas yield. Also generates lower levels of nitrogen than ADCA (between 10 - 20 %). For insulation materials its use is predicted to result in higher material density and higher thermal conductivity. Where used for insulation,	The greater quantities of material required would occupy increased processing / production and storage space and is expected to result in higher prices for the end consumer. It is considered to be between ten and up to twenty times more expensive than ADCA.		Substance is flammable. Relevant Classifications [Notified classification and labelling health and environmental hazards]: H302 Harmful if swallowed H315 Causes Skin irritation H319 Causes serious eye irritation H332 Harmful if inhaled. H335 May cause respiratory	Commercially available [Note 9] No EU producer.

Substance	Public document where it is identified as a potential alternative to ADCA	Technical feasibility	Economic feasibility	Applications mentioned / tested	Environment and human health hazards and risks	Availability
		significantly greater quantities of the material would be required (i.e. thicker insulation). Adverse effect on product quality of foamed products, in at least some applications.			irritation.	
3,7-dinitroso-1,3,5,7-tetraazabicyclo[3.3.1]nonane DNPT	Comments on Annex XV Dossier for identification a substance as an SVHC and response to those comments (ADCA). [Note 4]	Reasonable functionality in some applications and relatively versatile. For insulation materials its use is predicted to result in higher material density and higher thermal conductivity. Where used for insulation, significantly greater quantities of the material would be required (i.e. thicker insulation).	Basic raw material within similar price range as ADCA. Substantial investment at plant where it is used in place of ADCA due to safety issues (see right). Substantial reformulation costs. This is offset by the greater quantities of material required, which would occupy increased processing / production and storage space and is expected to result in higher prices for the end consumer.	Some medium density block foams. Some closed cell rubber applications (but some loss of functionality and potential loss of consumer acceptability). Some closed cell rubber applications (but some loss of functionality and potential loss of consumer acceptability).	Explosive. Dangerous and handling and processing. Limited data available. Formaldehyde is released during decomposition and is contained in the final product. Limited data available. Substance is flammable. Formaldehyde can be introduced in articles as a result of the use of the substance. It is also unstable if exposed to mineral acids or salts and releases a foul odour during processing and in the finished article. Relevant Classifications [Notified classification and labelling health and environmental hazards]: H302 Harmful if swallowed H315 Causes Skin irritation H319 Causes serious eye irritation H332 Harmful if inhaled. H335 May cause respiratory irritation.	Commercially available[Note 10]. No EU producer.

Substance	Public document where it is identified as a potential alternative to ADCA	Technical feasibility	Economic feasibility	Applications mentioned / tested	Environment and human health hazards and risks	Availability
					H341 Suspected of causing genetic defects	

Notes:

[1] Source: Guidance on the preparation of authorisations for application (ECHA). http://www.echa.europa.eu/documents/10162/13637/authorisation_application_en.pdf

[2] http://europe.marubeni.com/products/view/obsh-blowing-agent

[3] http://echa.europa.eu/documents/10162/d9e11c88-481a-47a9-8fff-915b48086ddb

[4] http://echa.europa.eu/documents/10162/bdd6746a-1905-4034-b456-c20dad47eeb2.[5] http://megaloid.ca/MSDS/Isopentane.pdf

[6] http://cameochemicals.noaa.gov/chemical/8744

[7] http://www.sigmaaldrich.com/catalog/product/aldrich/132004?lang=en&region=GB

[8] See for example: http://www.chemicalbook.com/ChemicalProductProperty_EN_CB3382662.htm (All producers listed are located in China); http://www.j-united.com/template/aboutus.htm (sites in Portugal but manufacturing appears to take place in China).

[9] http://www.chemexper.com/chemicals/supplier/cas/18039-42-4.html

[10] http://shivamadhesive.com/rubber-blowing-agent.html

6. Findings

The previous sections include a range of information that is likely to provide an improved understanding of the use of and exposure to ADCA in the EU. In order to support the ADCA task force with providing a response to ECHA's public consultation, some conclusions are drawn below on the potential implications against the criteria used in the prioritisation approach used to select substances for inclusion in Annex XIV[20].

Possible alternative scores have been provided taking into account the new information obtained through the survey as well as the fact that REACH registrations have recently been amended to remove registration of all consumer and professional use, and to remove certain industrial applications considered in the prioritisation process (e.g. industrial spraying) which, if they took place, could have led to more significant exposure.

Table 6.1 Summary of implications of additional information against aspects considered in prioritisation for ADCA

Aspect	Score (range)	Comments
Aspects with quantitative scoring		
Intrinsic properties	1 (0 – 4)	In the prioritisation process, a score of 1 is awarded for C or M substances without an effect threshold, and a score of 0 for C, M or R substances with an effect threshold. Based on the results that are available in the respiratory toxicity of ADCA, it appears that a safe concentration of exposure can be projected to be between 0.5 and 1.5 mg/m3 time weighted over an 8 hour work day. There are still numerous questions that need to be answered with regard to both the mechanisms of action and population heterogeneity before any statistical certainty can be attributed to these predictions. However, they are well in line with the experience in the UK where 8-hour maximum exposure limits of 1 mg/m3 in 1996 resulted in a complete halt to reported cases of occupational asthma associated with ADCA exposure. Possible alternative score = 0 if threshold defined, but assume 1.

[20] General Approach for Prioritisation of Substances of Very High Concern (SVHCs) for Inclusion in the List of Substances Subject to Authorisation, ECHA, 28 May 2010.

Aspect	Score (range)	Comments

Wide dispersive use	#sites = 3 (0 – 3)
	Release = 3 (0 – 3)
	Total = 3 x 3 = 9 (0 – 9)
		Number of sites:
		• In the prioritisation process, small (<10) = 1 point, medium (tens) = 2 points, high (hundreds) = 3 points.
		• The number of sites using ADCA is indeed in the hundreds. However, the number of sites using the substance in the form (ADCA powder) most likely to lead to highest levels of exposure is likely to be in the order of several tens.
		Release:
		• In the prioritisation process, insignificant = 0 point, non-diffuse / controlled = 1 point, diffuse / uncontrolled / significant = 3 points.
		• Based on the information on risk management measures applied (discussed above), it might be argued that the releases of ADCA are generally 'controlled'. This is defined as: "Releases at the workplace may occur but ... risk management measures are in place to control workplace exposure. It is however not clear whether the RMMs in place render workplace releases negligible".
		Possible alternative score = 2 for sites (if only ADCA powder considered) x 1 for release (if use is 'controlled') = 2

Volume, imports/exports	9 (0 – 9)	This relates to volumes of the substance within the scope of authorisation. For ADCA, it is unlikely that many of the uses are specifically exempted from authorisation. A score of 9 is awarded to substances supplied in volumes of >10,000 tonnes per year in the EU, which is the case for ADCA. Even though many of the end-users' processes use ADCA in a form likely to lead to lower levels of exposure than pure ADCA (e.g. low/zero dust), the quantity of pure ADCA powder imported into the EU is close to 12,000 tonnes per year, and almost all of this is supplied to uses that are not exempt from authorisation (e.g. formulation, compounding or use in production of articles). The score awarded to ADCA (9) therefore seems consistent with the relevant volume of ADCA on the market.
Total score	19	Possible alternative score = 12
Other aspects		
Geographical distribution of supply chain	-	The prioritisation document for ADCA highlighted the fact that there was no conclusive information available regarding the supply chain structure of the uses of ADCA in the scope of authorisation. The information presented in this report provides a more detailed understanding of the roles of different actors in the supply chain, the final products and the numbers of companies and (potentially exposed) employees.
Alternatives	-	Information provided by respondents to the survey indicates that none of the substances mentioned as possible alternatives are considered to be technically feasible for any of the main uses of ADCA
Existing specific EU legislation relevant for exemption	-	According to the prioritisation approach, this potential reason for not prioritising substances applies where "all identified uses are subject to specific Community legislation imposing minimum requirements relating to the protection of human health or the environment ensuring that risks are properly controlled." Whilst it could potentially be argued that worker protection legislation such as the chemical agents directive (98/24/EC) imposes minimum requirements relating to protection of human health, it could not credibly be argued that this legislation is "specific" to ADCA or the uses in which the substance is applied.

Aspect	Score (range)	Comments
Regulatory effectiveness	-	The 'second tier' approach to considering regulatory effectiveness is relevant where inclusion in Annex XIV will require regulatory efforts but most likely will not result in benefits for human health or the environment, or where use of other risk management instruments may be hampered while not contributing significantly to achieving the risk reduction (cf. Section 2.3 of the general approach to prioritisation). Based on the information analysed in relation to ADCA, the following conclusions are drawn: • Authorisation would likely lead to significant regulatory efforts e.g. cost implications in terms of developing applications and, if unsuccessful, to costs related to loss of business activity in the EU and/or consequential costs associated with use of alternatives (e.g. reduced energy efficiency). • In terms of benefits from human health from reduced exposure to ADCA, it is likely that these will mainly relate to any users which (a) use forms of the substance likely to cause high levels of exposure (e.g. pure ADCA dust) and (b) do not apply the risk management measures specified in the registration dossier for the substance. Given steps over recent years by users of ADCA to introduce more stringent RMMs, and the reduction in numbers of reported adverse effects, health benefits are likely to be limited to a rather small number of firms and employees. • Moreover, there may potentially be increased health risks from the use of alternatives to ADCA, although only the hazards of alternatives have been reviewed in this note. • It is not clear that any other risk management instruments would be 'hampered' through a requirement for authorisation of ADCA. However, given that there are significant differences in exposure according to the form of the substance used, the merits of requiring authorisation for e.g. use of ADCA in zero-dust or paste form, for example, may not be clear compared to other possible approaches (e.g. a binding occupational limit value under Directive 98/24/EC). • It is clear from the information collected during the survey that there could be very significant socio-economic impacts if companies are no longer able to use ADCA, given the apparent lack of any suitable alternatives, and the ability for non-EU firms to continue to sell ADCA-foamed articles on the EU market regardless of whether an authorisation requirement is introduced.

See ECHA general approach for prioritisation of SVHC: http://echa.europa.eu/documents/10162/13640/axiv_priority_setting_gen_approach_20100701_en.pdf. Scores included in the second column are those included in the draft background document for ADCA of 24 June 2013.

Appendix A
Survey of ADCA Task Force Members and their customers in the Context of Possible inclusion in the Authorisation list under REACH ("ADCA Survey")

In order to collect up-to-date and relevant information for the response to ECHA's public consultation. AMEC, contracted by ReachCentrum, developed a questionnaire for the ADCA Task Force members. Where practicable within the timeframes specified for the public consultation, the task force members invited their suppliers and customers to provide responses to the questionnaire. The companies provided information on:

- The inputs to their business which contain ADCA, including the volume of inputs (tonnes per year) and the concentration of ADCA in these. Data has also been provided on the outputs from each company which contain (or are based on) ADCA, along with the concentration of ADCA in these products. This data has enabled an analysis of the total volumes of ADCA used for various processes and to 'trace' the total ADCA volume through the different stages in the supply chain to the final articles. (The data provided are considered to cover the majority of the market in terms of importers of the substance, and a majority also in terms of quantities of ADCA used by downstream users.)
- How and why Task Force members use ADCA (and mixtures containing the substance) and its importance to their business and to their customers.
- How Task Force members and their customers would respond if the substance were included on Annex XIV and no authorisation was received for some or all of the uses of the substance.
- How substances that are marketed (or have been identified) as potential alternatives to ADCA compare in terms of their technical feasibility, cost, availability and other impacts.

AMEC and ReachCentrum sent the questionnaires (one to each member, some of whom subsequently circulated the questionnaire further) to Task Force members on 1 August 2013, and Task Force members provided information to AMEC with a deadline of 23 August 2013. The level of detail contained in this report reflects these timescales. More detailed information and further analysis are likely to be available, given longer timescales.

Companies were asked to state their role in the supply chain, which included category 1 (importers of ADCA); category 2 (distributor of ADCA or mixtures containing the substance); category 3 (formulators of mixtures / masterbatches containing ADCA); category 4 (compounding of ADCA); and category 5 (end processor / producer of articles using ADCA). A small number of companies classified themselves as 'other', which includes those who export the product into the EU (the corresponding volumes were not included in the analysis so as to avoid double counting).

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Doc Reg No. 34359CA002i3

Companies were asked to describe the key stages in the supply chain relevant to their product(s) containing ADCA; the processes undertaken by their firm; the outputs from this, along with volumes and concentrations of ADCA in their products/articles. They were asked to describe the functionality of ADCA and the benefits to them of its use. The survey also collected various socio-economic information, and details of alternatives considered (if any) and the implications for their business of a potential loss of the substance.

The survey collected data on employee exposure, including the form of ADCA employees were exposed to, the concentration and duration of exposure. Details of relevant risk management measures (RMMs) were also collected.

In total, 81 companies provided inputs related to their use of ADCA. This represents a very good response rate given that the timescales for provision of information were short and some companies would have been unable to respond due to lack of resources to participate in the survey and the timing of the consultation over the summer holiday period. Comparing the import volumes of ADCA, to the use of the substance in later stages of the supply chain, suggests the survey data covers a significant proportion of the market.

These 81 companies represent total annual EU sales turnover from products containing ADCA of some €2.5 billion.

Appendix B
References for Toxicological Analysis

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