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Research to determine the incidence, prevalence and relative risk of ill health due to chemical exposure in the chemical and downstream oil industry sector

Prepared by the **Health and Safety Laboratory**
for the Health and Safety Executive 2014

RR1013
Research Report

HSE

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Research to determine the incidence, prevalence and relative risk of ill health due to chemical exposure in the chemical and downstream oil industry sector

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This project identified seven data sources from which to assess ill health problems potentially associated with exposure to harmful chemicals in the chemical and downstream oil industry. Interrogation of these sources allowed insight into the range and type of ill health previously, and currently, associated with certain exposures. A bespoke definition of the chemical and downstream oil industry sector, based on SIC codes, was developed as part of this project in order to assist this process.

It was written to:

- define the scope of the term 'Chemical Sector'.
- review and critically appraise the data sources of reported ill health and related exposure data in order to better understand these relationships in the chemical sector.
- undertake a scoping review of the peer reviewed published literature to establish the range and type of reported industry sector causes of occupational ill health due to chemicals.
- use this information to identify which particular industries within the chemical sector may have previously described high levels of work-related ill health.

This report and the work it describes were funded by the Health and Safety Executive (HSE). Its contents, including any opinions and/or conclusions expressed, are those of the authors alone and do not necessarily reflect HSE policy.

HSE Books

First published 2014

KEY MESSAGES

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Overall, 2006/7 – 2010/11 data from the self-reported work-related illness part of the LFS identified that the average rate (per 100,000) of all ill health due to occupation was found to be 2880 within the chemical and downstream oil industry, compared to 3470 for all industries and 3060 for the manufacturing sector, of which the chemical and downstream oil industry is a part.

Ill health problems related to chemical exposure included occupational asthma and dermatitis, certain occupational cancers, and a group of other miscellaneous conditions.

Occupational asthma was a relatively commonly reported ill health consequence of chemical exposures in both the RIDDOR and THOR schemes. Main causes included aldehydes, enzymes, soaps and detergents, isocyanates, laboratory animals and sewerage, pharmaceuticals, dyes and pigments and metals/metal compounds. SWORD data noted that the annual estimated rate of occupational asthma for the manufacture of chemicals and chemical products division of the chemical sector was similar to the estimated rate for the manufacturing sector, and higher than the estimated rate for all industries combined.

Occupational dermatitis was also a commonly reported ill health consequence of chemical exposures in both the RIDDOR and THOR schemes. Main causes included pharmaceutical agents, soaps and detergents, acrylic resins, epoxy resins, hardeners, cosmetics and toiletries, wet work, dyes and pigments, preservatives, rubber chemicals and materials and enzymes. THOR data noted that the annual estimated rate of occupational dermatitis for the manufacture of chemicals and chemical products division of the chemical sector was higher than the estimated rate for both the manufacturing sector and all industries combined.

Occupational cancer: certain cancers were identified that had significant occupational associations. Whilst data strength varied across data source, gender and cancer type, the following were generally identified as relevant to chemical sector exposures: bladder, breast, larynx, leukaemias (Chronic Lymphatic Leukaemia and others), liver, lung, meningeal, mesothelioma, rectal, sino-nasal, soft tissue sarcoma and stomach.

Finally, the literature review identified various other conditions related to exposure to chemicals, in addition to those described, including uncommon lung disease (e.g. caused by diacetyl exposure, opiates, phthalates), chemical induced hearing loss, neuro-developmental issues, chronic toxic encephalopathy and reproductive health issues.

Can these findings be generalised to other populations? Findings from each of the data sources will have differing levels of generalisability, given the nature of each data source. For example, RIDDOR and THOR data are likely to reflect local GB context, whilst Cancer Burden and Decennial Supplement data may be more applicable to other working populations.

Historic and current exposure to chemicals in the industry sector are associated with the development of ill health, and these findings will hopefully assist future strategy development to reduce new cases of ill health due to exposure to chemicals.

EXECUTIVE SUMMARY

During the period 2006 to 2011, there were approximately 281,000 workers employed per year in the chemical and downstream oil industry. These and more recent 2011 figures suggest that chemical workers represent approximately 9% of all workers employed in the manufacturing industry.

The predominant role of the chemical and downstream oil industry is to chemically transform natural materials into products of added value. The starting materials are normally mixes of minerals, metals and hydrocarbons, from which intermediate and finished chemical products are manufactured.

These chemical exposures have potential to cause a variety of human diseases, although the exact size of this effect on ill health is currently difficult to assess accurately. The aim of this project was to determine the incidence (new cases of ill health or disease), prevalence (current numbers of ill health or disease cases) and relative risk of ill health in workers due to, or attributed to, exposure to chemicals in the chemical and downstream oil industry sector. In order to achieve this aim, a number of specific objectives were identified; these were: (1) to define the scope of the term "Chemical Sector", (2) to review and critically appraise the data sources of reported ill health and related exposure data in order to better understand these relationships in the chemical sector (3) to undertake a scoping review of the peer reviewed published literature to establish the range and type of reported industry sector causes of occupational ill health due to exposure to chemicals.

(1) Definition and scope of the chemical sector: in order to develop this, the HSE definition of the chemical sector, taken from the chemical sector strategy, was used as a starting point. United Kingdom (UK) SIC codes (Standard Industrial Classification of Economic Activities) were then identified for each of the areas identified by HSE. The subsequently compiled list of SIC codes constituted the chemical sector classification and were used subsequently within this project to aide searching data sources for chemical-related ill health issues.

(2) Review and critical appraisal of data sources of reported ill health and related exposure: seven data sources were identified and subsequently assessed. These were (i) RIDDOR (Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995) disease notifications, (ii) SWI (Self-reported Work-related Illness) reports from the LFS (Labour Force Survey), (iii) disease notifications made under THOR (The Health and Occupation Research network), (iv) the HSE funded Cancer Burden Project, (v) the latest two occupational health decennial supplements, (vi) the NEDB (National Exposure Data Base) and (vii) industry data supplied by the Chemical and Downstream Oil Industry Forum (CDOIF).

(i) RIDDOR: potentially reportable conditions under the RIDDOR regulations fall into 72 disease categories. Summary details of disease incidence notifications made under RIDDOR (1995) within the chemical sector were obtained from HSE. A total of 9937 disease reports, covering all industries, were made over the period 2006/07 to 2010/11; of which 207 were from the chemical sector. Approximately 2% of all reported diseases, 6% of all occupational asthma reports and 8% of all occupational dermatitis reports were made by the chemical sector.

Over the 5-year period, 10% of reports made by the chemical sector were for occupational asthma, compared to 3% of reports made by other sectors. Over the same period, 53% of reports made by the chemical sector were for occupational dermatitis, this compared to 13% of reports made by other sectors.

(ii) SWI data: the average prevalence rate (point estimate per 100,000) of all ill health due to occupation was found to be 2880 within the chemical sector, compared to 3470 for all industries and 3060 for the manufacturing sector (of which the chemical sector is a part). However, the confidence intervals for these prevalence rates overlapped, and therefore no evidence of a significant difference could be found.

(iii) THOR data: occupational asthma and dermatitis were the predominant diagnoses reported to THOR from within the chemical sector. The annual estimated incidence rate of occupational asthma for the "manufacture of coke, refined petroleum products and nuclear fuel" division of the chemical sector, as reported to SWORD, was higher than the estimated incidence rates for both the manufacturing sector and all industries combined. The annual estimated incidence rate of occupational asthma for the "manufacture of chemicals and chemical products" division of the chemical sector, as reported to SWORD, was similar to the estimated incidence rate for the manufacturing sector and higher than the estimated incidence rate for all industries combined. The annual estimated incidence rate, as reported to OPRA, was higher than the estimated incidence rates for both the manufacturing sector and all industries combined.

The annual estimated incidence rate of occupational dermatitis for the "manufacture of coke, refined petroleum products and nuclear fuel" division of the chemical sector, as reported to EPIDERM, was similar to the estimated incidence rate for the manufacturing sector and higher than the estimated incidence rate for all industries combined. The annual estimated incidence rate of occupational dermatitis for the "manufacture of chemicals and chemical products" division of the chemical sector was higher than the estimated incidence rate for both the manufacturing sector and all industries combined, as reported to EPIDERM and OPRA.

When considering RIDDOR and THOR sources together, the main associations reported for occupational asthma included aldehydes, enzymes, soaps and detergents, isocyanates, laboratory animals and sewerage, pharmaceuticals, dyes and pigments and metals/metal compounds. The main associations reported for occupational dermatitis included pharmaceutical agents, soaps and detergents, acrylic resins, epoxy resins, hardeners, cosmetics and toiletries, wet work, dyes and pigments, preservatives, rubber chemicals and materials and enzymes. An association with occupational dermatitis was also identified for the use of personal protective equipment (PPE).

(iv) Cancer Burden data: many data were available for consideration, the details of which are given in the main report. Given the long latency nature of most cancers, these findings largely relate to historic exposures at work. In brief, the largest attributable fractions (proportion of cancer incidence and mortality that could be attributable to occupational exposures) across the chemical sector were found for mesothelioma (pleural cancer) and lung cancer attributable to asbestos exposure (in petroleum refineries, manufacture of industrial chemicals and manufacture of other chemical products) and laryngeal cancer attributable to exposure to strong inorganic acid mists containing sulphuric acid (in manufacture of industrial chemicals and manufacture of other chemical products).

After these, sino-nasal cancer attributable to wood dust exposure (in the manufacture of industrial chemicals and manufacture of other chemical products), soft tissue sarcoma attributable to TCDD exposure (in the manufacture of industrial chemicals) and liver cancer attributable to exposure to vinyl chloride (in the manufacture of industrial chemicals and manufacture of other chemical products) had the largest attributable fractions. As well as these cancer/agent combinations, the highest estimated numbers of attributable cancer registrations and deaths were for lung cancer attributable to exposure to strong inorganic acid mists (containing sulphuric acid) and cobalt exposure.

The original peer reviewed publications considered by the Cancer Burden Project were assessed in detail for strong inorganic acid mists and laryngeal cancer, strong inorganic acid mists and

lung cancer, vinyl chloride and liver cancer and cobalt and lung cancer. It was evident that the individual risk estimates from studies varied, presumably as a consequence of differing study designs, study populations and geography and exposure assessments.

(v) Occupational Health Decennial Supplement data provided risk estimates of various causes of mortality stratified by occupation.

In relation to chemical engineers and scientists: in the 1995 occupational health decennial supplement the greatest mortality risk for men was from cancer of the pleura and the greatest cancer risk for men was from chronic lymphatic leukaemia. There were no significantly elevated mortality or cancer risks for women. In the 2009 update of occupational mortality, a significant excess mortality risk of cancer of the pleura remained for men.

In addition to cancer of the pleura, an increased mortality risk for meningeal tumour and multiple sclerosis was found for men. In women, there were increased mortality risks for peripheral vascular disease and cancer of the rectum identified.

In relation to chemical workers: in the 1995 occupational health decennial supplement there was a high death rate from pleural cancer for both men and women. The greatest mortality risk for men was from poisoning by "other gases". There were also high mortality risks for death due to injury from accidents involving explosive material, hot substances and machinery. The greatest cancer risk for men was from cancer of the pleura. For women, there was an increased cancer risk for all leukaemia and for stomach cancer.

In the 2009 update of occupational mortality, a significant excess mortality risk of urothelial cancer was reported for men and an excess mortality risk of ischaemic heart disease was reported for women. The mortality risk for cancer of the pleura was no longer elevated in men or statistically elevated in women. The elevated mortality risk from accidents possibly related to work in men remained (although not significantly) for injuries due to explosive material, poisonings by "other gases" and hot substances.

In addition to urothelial cancer, an increased mortality risk for cancer of the stomach and ischaemic heart disease was found for men. In women an increased mortality risk for hypertensive disease was identified.

(vi) NEDB data available from 2006-11 were limited to specific workplace exposure measures. Data were available relating to cobalt only; of the three categories specifically identified from the Cancer Burden Project (cobalt, strong acid mists, vinyl chloride), although other workplace measures were available from the chemical sector, these included measures of azodicarbonamide, total chromium, hexavalent chromium, gluteraldehyde, hydrazine and methylene biphenyl di-isocyantate, xylene and trichloroethylene.

(vii) The CIA kindly supplied a framework of ill health conditions that have information recorded about reported illness in the sector. Future work in this area could include specific focus on one or more of these areas.

(3) The literature review findings were broadly consistent with the findings from the other data sources, although no comprehensive reviews of the ill health effects of chemical exposures were identified. In addition to the anticipated findings related to asthma and various links to cancer, a set of miscellaneous conditions were identified. These included uncommon lung disease (e.g. potentially caused by diacetyl exposure, opiates, phthalates), health issues in pharmaceutical workers, chemical induced hearing loss, neuro-developmental issues, chronic toxic encephalopathy and potential adverse reproductive health.

A summary of major diseases identified and the relevant source is shown in Table i.

Table i Breakdown of main disease categories and data sources supporting causation in the chemical sector (gender not considered individually, main reported substances only listed)

Disease type	Associated exposures	Notes
Occupational asthma	Isocyanates	b
	Aldehydes; (including formaldehyde, glutaraldehyde)	b
	Enzymes	a,b
	Laboratory animals and sewerage	b
	Pharmaceuticals	b,f
	Soaps and detergents	a,b
	Dyes and pigments	b
	Metals and compounds	b
Other airway/lung	Opiates	f
Airway responses to;	Phthalates	f
Bronchiolitis	Diacetyl	f
Occupational Dermatitis	Pharmaceutical agents	a,b,f
	Soaps and detergents	a,b
	Acrylic resins, epoxy resins and hardeners	a,b
	Preservatives	a,b
	PPE contribution	a,b
	Rubber chemicals and materials	a,b
	Metals and compounds	b
	Cosmetics and toiletries	a,b
	Organic solvents	a,b
	Enzymes	a
Cancers		
Lung Cancer	Asbestos, cobalt, strong inorganic acid mists	c
Laryngeal cancer	Strong inorganic acid mists	c
Mesothelioma	Asbestos	c,d,e
Bladder	Various urinary carcinogens	e,f
Sino nasal	Wood dust	c
Soft tissue sarcoma	TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin)	c
Liver	Vinyl chloride	c
Meningeal tumour	Exposure not identified	e
Stomach	Exposure not identified	d,e
Rectal	Exposure not identified	d
Breast	Pharmaceutical workers	f
CLL	Exposure not identified	d
All leukaemias	Exposure not identified	d
Other conditions		
Death from poisoning	"other gases"	d
Accidents	Involving explosive materials and machinery	d
Multiple sclerosis	Exposure not identified	e
Peripheral vascular disease	Exposure not identified	e
IHD*	Exposure not identified	e
Hypertension	Exposure not identified	e
Chemical induced hearing loss	Including toluene, styrene, solvent mixtures, carbon monoxide	f
Neuro-developmental issues	Including arsenic lead, methyl mercury, toluene, PCBs	f
Chronic toxic encephalopathy	Organic solvent exposures	f
Reproductive health	Phthalates	f

a=RIDDOR, b=THOR, c=Cancer Burden data, d=Decennial Supplement 1995, e=Decennial Supplement 2009, f=Literature Review
*Ischaemic Heart Disease

CONTENTS

1. INTRODUCTION

During the period 2006 to 2011, there were approximately 281,000 workers employed per year in the chemical and downstream oil industry, based on data from the Annual Population Survey (APS) obtained from the Office for National Statistics (ONS)[1]. Also over this period, it is estimated that there were approximately 3,061,000 workers employed in the manufacturing industry, and 28,187,000 workers employed over all industries.

It is estimated that the corresponding numbers for 2011, taken from the most recent annual estimate available, are approximately 248,000 workers employed in the chemical and downstream oil industry, 2,749,000 workers employed in the manufacturing industry and 28,160,000 workers employed in overall in Great Britain. These figures suggest that chemical workers represent approximately 9% of all workers employed in the manufacturing industry, and 1% of workers overall in Great Britain (GB).

The Annual Population Survey (APS) combines data from the Labour Force Survey (LFS) and national boosts. The increased sample size enables more robust estimates to be produced and seasonal biases to be removed. The figures reported here will differ from the official ONS Labour Market Statistics, whose estimates are based on the LFS rather than the APS, and the UK rather than GB. Further information on the ONS Labour Market can be found on the ONS website.

The predominant role of the chemical and downstream oil industry is to chemically transform natural materials into products of added value. The starting materials are mixes of minerals, metals and hydrocarbons, from which intermediate and finished chemical products are manufactured. The main chemical products developed are basic inorganics, basic organics, fertilizers and pesticides, plastics, resins, synthetic rubbers, cellulosic and synthetic fibres, pharmaceuticals, paints, varnishes and lacquers, soaps, detergents, cleaning preparations, perfumes, cosmetics and other toiletries and other miscellaneous chemicals. During the process stages used to develop these products, storage and delivery of chemical materials, exposure of workers by skin contact, inhalation or ingestion may occur.

These exposures have potential to cause a variety of human diseases, although the exact size of this effect is currently difficult to assess accurately. Certain data already exist to assist with this assessment. For example, 2008-2010 data from the GB based THOR (The Health and Occupation Research network) scheme indicate that the annual average reported numbers of occupational asthma and dermatitis were higher in chemical manufacturing than in all industries combined. In addition, over the same time period, and using all the 2-digit SIC 2003 codes, chemical manufacturing had the 7th highest incidence of occupational asthma and 4th highest incidence of dermatitis[2]. Whilst it is recognised that THOR data relates to individual case reporting, these data suggest that a more comprehensive assessment of other sources of relevant data is justified.

Additionally, results from the Health and Safety Executive's (HSE) interim overview report published in 2010 on the Burden of Occupational Cancer in Great Britain[3] identified that the work category "Manufacture of industrial chemicals" ranked 14th out of all 60 industries for attributed cancer deaths (103 attributable deaths) and ranked 19th out of all 60 industries for attributed cancer registrations (121 attributable registrations). The report also identified the work category "Manufacture of other chemical products" ranked 13th out of all 60 industries for attributed cancer deaths (107 attributable deaths), and ranked 18th out of all 60 industries for attributed cancer registrations (123 attributable registrations). These values combined suggested

that overall chemical manufacturing was responsible for 2.6% of attributable cancer deaths and 1.8% of attributable cancer registrations.

The overall aim for HSE's chemical sector strategy is to reduce the incidence of work-related ill health linked to chemical exposure. Given the suggestion that the chemical sector may be responsible for relatively high numbers of work-related ill health, and the fact that recent relevant studies commissioned by HSE and awareness raising campaigns have not been focussed on the chemical sector, further exploration of the evidence base is presented here. The eventual aim of such work is to enable better, and more targeted intervention activity where appropriate.

1.1 PROJECT AIM

The aim of this project was to determine the incidence (new cases of ill health or disease), prevalence (current numbers of ill health or disease cases) and relative risk of ill health in workers due to, or attributed to, chemical exposure in the chemical and downstream oil industry sector.

1.2 OBJECTIVES

There were four project objectives.

(1) To define the scope of the term "Chemical Sector".

(2) To review and critically appraise the data sources of reported ill health and related exposure data in order to better understand these relationships in the chemical sector.

(3) To undertake a scoping review of the peer reviewed published literature to establish the range and type of reported industry sector causes of occupational ill health due to chemicals.

(4) To use information from (2) and (3) to identify which particular industries within the chemical sector may have previously described high levels of work-related ill health.

2. IMPLICATIONS

This work aimed to determine the incidence, prevalence and relative risks of ill health in workers due to, or attributed, to chemical exposures in the chemical and downstream oil industry. In order to achieve this, an additional requirement of this research was to define the scope of the chemical sector.

Seven potential data sources were identified to assist with this process, and four of these contained useful data with a combination of health effect and some exposure information (RIDDOR, THOR, Cancer Burden data and ONS decennial supplement data).

The review of data sources that contained health and exposure information generally identified health end points associated with chemical exposures that are established and already identified to be risks.

Examples included:

- Occupational asthma due to isocyanates, aldehydes, enzymes, laboratory animals and sewerage, pharmaceutical agents, soaps and detergents, dyes and pigments and metals.
- Occupational dermatitis due to pharmaceutical agents, soaps and detergents, acrylic and epoxy resins, hardeners, preservatives, rubber associated chemicals and materials, metals and wet work.
- Occupationally related cancers; in particular where exposures are identified; lung cancer (asbestos, cobalt, strong inorganic acid mists), laryngeal cancer (strong inorganic acid mists), mesothelioma (asbestos), bladder (various carcinogens in urine), sino-nasal (wood dust), soft tissue sarcoma (TCDD), and liver (vinyl chloride).

Various considerations have to be taken into account when interpreting the information. Certain sources, for example RIDDOR and THOR, were based on data that required respectively employers and doctors to identify and report cases to these schemes. These schemes may not capture all cases of a particular illness, and hence may under report. These sources may therefore find less cases than are actually occurring.

In terms of the scientific findings of the study, the most useful data sources combined measure of a health end point and at least some knowledge of the chemical exposure. The latter could be either a reported agents, or in the case of the cancer burden data, measured values taken from previous peer reviewed publications. For further burden estimates to be possible in future, similar data combining measure of a health end point and some knowledge of the chemical exposure would need to be gathered in current studies of ill health.

3. METHODOLOGY

The methodology section is divided into three discrete areas, aligning with the aims and objectives for this project. These are; (1) definition of the chemical sector, (2) review of individual data sources and (3) review of peer reviewed literature.

3.1 DEFINITION OF THE CHEMICAL SECTOR

For the purpose of this project, HSE's definition of the chemical sector from the chemical sector strategy was used as a starting point. United Kingdom (UK) SIC codes (Standard Industrial Classification of Economic Activities) were then identified for each of the areas identified by HSE. SIC codes are based on a hierarchical five-digit system that classifies business establishments and other statistical units by the type of economic activity in which they are engaged.

The subsequently compiled list of SIC codes constituted the chemical sector classification. These are shown, along with the original HSE definition, in Appendix 1. The resulting SIC codes are briefly discussed further in the results section.

3.2 REVIEW OF INDIVIDUAL DATA SOURCES

Seven data sources were identified for this part of the project, given the varied nature of the seven data sources, a combination of incidence (new cases of ill health or disease), prevalence (current numbers of ill health or disease cases) and risk data are shown. There were some limitations when interpreting each of the data sources; these are highlighted in the relevant result section.

Three of the data sources were obtained and used following external consultation with HSE. These were (i) RIDDOR (Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995) disease notifications, (ii) SWI (Self-reported Work-related Illness) reports from the LFS (Labour Force Survey) and (iii) disease notifications made under THOR.

Data from the (iv) Cancer Burden Project were obtained from colleagues within HSL (Health and Safety Laboratory) and data for the (v) latest two occupational health decennial supplements were obtained from published reports and the ONS (Office for National Statistics) website.

Information on chemical exposure within the chemical sector was obtained from the (vi) National Exposure Data Base (NEDB) and (vii) industry contacts made at a Chemical and Downstream Oil Industry Forum (CDOIF) meeting and Chemicals Industries Association (CIA) event.

Data from RIDDOR, SWI and THOR were obtained covering the 5-year period 2007-2011 for the chemical sector, the manufacturing sector and all industries combined. Detailed data, where available, were obtained for the chemical sector only. Generally the following detailed information was requested from the three datasets: records covering the period 2006/07 to 2010/11, records covering the chemical sector only and certain individual case based data. The latter included information where possible in relation to occupation, illness/disease, exposure/agent and industry.

(i) Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995 (RIDDOR)

RIDDOR is a national GB based reporting scheme that collects reports on workplace incidents, including deaths of workers or members of the public and injuries to workers arising from a work activity, selected incidents that have a high potential to cause death or serious injury (whether or not someone is injured) and prescribed diseases. RIDDOR reporting is a legal requirement under the Health and Safety at Work Act 1974, and cases are reported by the duty holder, not by health care professionals.

Potentially reportable conditions under the RIDDOR regulations fall into 72 disease categories. These broadly fall into four groups; conditions due to physical agents and the physical demands of work, infections due to biological agents, conditions due to substances and additional diseases to be reported with respect to offshore work places. Details of the diseases within these groups can be found in Appendix 2. Further information on the regulations and the work activities associated with the reportable diseases can be found on the HSE RIDDOR website.

RIDDOR consequently provides an indication of the incidence of work-related ill health.

For the purposes of this particular project, disease notifications made under RIDDOR within the chemical sector were the particular focus. Summary details of disease notifications made under RIDDOR 1995 were obtained from the relevant department within HSE. Detailed records were obtained from the RIDDOR database for all reported diseases within the chemical sector, specifically using the SIC codes associated with the chemical sector definition as developed in this project. Information was obtained on industrial activity, reported disease and a free-text description providing details of the diagnosis and cause(s); where provided by the individual case notifier.

The free-text descriptions for selected diseases were examined by an occupational health expert to determine the leading substance/exposure(s) likely to be associated with the reported diagnosis. Due to the nature of the reporting process, information on the specific occupation of the particular individual worker reported was not available.

(ii) Self-reported Work-related Illness (SWI) Survey

The Labour Force Survey (LFS) is a representative national survey of private households in the UK. The survey provides information on the UK labour market, and is managed by the Office for National Statistics (ONS). HSE commissions questions in the LFS to obtain information on perspectives of work-related illness and workplace injury. These questions are included in two modules of the LFS; “The workplace injury survey” and the “Self-reported Work-related Illness (SWI) survey” respectively.

Individuals are asked to self-report any illness over the previous 12 months that they believe is caused, or made worse by, their occupation or workplace. Individuals are asked how many work-related illnesses they had suffered from, in their opinion, and asked to provide details for the “most serious”. The SWI survey collects details on several illnesses, including musculoskeletal disorders, respiratory and skin problems; a full list of all self-reported conditions can be found in Appendix 3.

The SWI survey consequently provides an indication of annual prevalence of work-related illness.

For the purposes of this project, analysis of work-related illness from the SWI was undertaken by HSE on behalf of HSL. The LFS survey data was used to make inferences about the whole GB population. Analyses were carried out on data for the period 2006/07-2010/11, and additionally for the 7-year period 2005/06-2011/12 and 9-year period 2003/04-2011/12; the additional analyses had larger samples and thus allowed more estimates to be produced. The chemical sector was also broken down into broad occupation categories based on Standard Occupational Classification (SOC) codes: office based, laboratory based, factory/warehouse based and an "other" category. Detailed records for the SWI (LFS) data could not be obtained by HSL due to the data access agreement between HSE and ONS. As a consequence, no further analysis or data investigations could be carried out beyond that carried out by HSE.

(iii) The Health and Occupation Research (THOR) Network

The THOR network is a surveillance scheme, within which specialist doctors and general practitioners are asked to voluntarily report new cases of work-related ill health to the project team, based at the Centre for Occupational and Environmental Health (COEH), Manchester University. The scheme provides estimates of the incidence and trends of occupational diseases based on specialist diagnoses. Further information can be found on the COEH THOR website.

The overarching THOR scheme includes the following surveillance schemes of interest for this project: Surveillance of Work-related and Occupational Respiratory Disease (SWORD), Occupational Skin Surveillance scheme (EPIDERM), Occupational Physicians Reporting Activity (OPRA), and reports by General Practitioners with training in Occupational Medicine (THOR-GP).

Estimated number of incidence cases and incidence rates of occupational ill health reported to THOR were obtained from the COEH[4] for SWORD, EPIDERM, OPRA and THOR-GP within the chemical sector, using the SIC codes associated with the chemical sector definition developed in this project. Information was obtained on industrial activity, reported diagnosis and reported agent cause as originally extracted by the THOR team from the information supplied by the case reporter.

The reported diagnoses were then examined by an occupational health expert to determine broad diagnosis categories. The reported agents were also examined by the same expert to determine the leading substance/exposure(s) potentially associated with the diagnosis from the case information supplied.

(iv) Cancer Burden Project

A collaborative project between Imperial College London (ICL), the Institute of Occupational Medicine (IOM), Institute of Environmental Health (IEH) and HSL was commissioned and funded by HSE to produce an updated estimate of the current burden of occupational cancer for GB. Attributable fractions (the proportion of cases of cancer that would not have occurred in the absence of occupational exposure) were used to estimate the current burden of cancer from historical occupational exposures. Subsequently, estimates of attributable numbers of cancer registrations in 2004 and cancer deaths in 2005 were calculated.

In 2012, finalised results for the burden of occupational cancer in Great Britain were released[5]. These updated results included an overall report similar to the interim report released in 2010 and 23 technical reports providing detailed results for individual cancer types.

Cancer burden data consequently provides an indication of work-related cancer incidence and mortality.

Detailed data from the HSE Cancer Burden Project, that were not previously published, were obtained from the HSL cancer burden study team. These data included the attributable fractions and estimated number of attributable cancer registrations and deaths by agent and industry for each individual cancer. For the purposes of this project results from the individual technical reports and the detailed data were assessed specifically to provide an indication of which cancers and agents may pose the greatest occupational risk to workers in the chemical and downstream oil industry.

(v) Occupational Health Decennial Supplement

The Occupational Health Decennial Supplement (OHDS) provides risk estimates for causes of mortality stratified by occupation. The main source of data for calculating these estimates is the national registration systems of England and Wales, within which information on sex, age, underlying cause of death and last occupation is extracted from death certificates.

Underlying causes of death are then grouped into broad diagnostic categories according to the likelihood of being caused by occupational exposures. Occupation is also grouped into broad job groups, according to the likely differences between work-related exposures.

The first Occupational Health Decennial Supplement considered reported mortality (over the periods 1979-1980 and 1982-1990) and cancer incidence (between 1981 and 1987) in men and women aged 20-74 years in England[6]. The most recent Occupational Health Decennial Supplement reported mortality for the period 1991-2000 in men and women aged 16-74 years in England[7].

Figures were extracted from the two final reports, and, in addition, further published data for the 2009 report were identified in the form of supplementary tables from the ONS website. The supplementary tables illustrated the number of deaths by cause in all occupation groups for men and women. The available data were presented as stratified by age groups; 16-64 / 65-74 years for men and 16-59 / 60-74 years for women. These available data were subsequently combined by a statistician for the purposes of this project to provide additional estimates of interest for this project, for the complete age range 16-74 years. In addition, the data were first used to reproduce the estimates included in the published reports to ensure that the process was applied appropriately.

Proportionate Mortality Ratios (PMRs) were used to compare mortality from particular causes of death among occupational groups to that of the general population. Proportional Registration Ratios (PRRs) were used to compare registrations from particular cancers among occupational groups to that of the general public. PMRs and PRRs were adjusted for age and social class; PRRs were also adjusted for the region of cancer registration. Only causes with significantly raised associations (and with at least 3 observed cases) or significantly low associations (and with at least 3 expected cases) were considered for the purposes of this project.

(vi) National Exposure Data Base (NEDB)

The industry sectors that make up the Chemicals Sector in the NEDB are shown in Appendix 7. These sectors were searched within the NEDB using the strategy described below, for the period 2006 – 2011.

A focussed and a more generic search were carried out. The focused search strategy used for the purposes of this project was to search the NEDB to align any outputs with the findings from the reviews of the other data sources identified in this work (and particularly the findings of the Cancer Burden Project). Accordingly, NEDB searches were requested for exposure data to

strong inorganic acid mists containing sulphuric acid (lung and laryngeal cancer attributed to this exposure), vinyl chloride (liver cancer attributed to this exposure) and cobalt (lung cancer attributed to this exposure). These three areas were specifically identified to be of interest as these three agents were responsible for highest percentage of attributable cancers in the chemical sector.

The NEDB was also generically searched for all other exposure data collected in the Chemical Sector Industries as defined in Appendix 7.

(vii) Industry Data

The project team discussed many potential sources of data specifically derived from industry, and it was concluded that whilst industry data do exist, there would need to be a specific intent for capturing specific data to test particular assumptions or other associations. However, a structure of data routinely recorded within industry was received, with thanks, from the Chemical Industries Association (CIA). This structure is shown in the results section.

3.3 REVIEW OF PEER REVIEWED LITERATURE

In order to carry out the scoping review of peer-reviewed literature, an agreed set of search terms were developed within the project team that were consistent with the stated aim of this part of the work. The aim of this particular component of this project was to establish the range and type of occupational ill health that has been attributed to exposures within the chemical sector.

The search period used was between 2002 and 2012, and the search was carried out by the HSE Information Centre. Details of the search strategy are given in Appendix 8. Search algorithms were prepared using specific disease terms that were anticipated to be relevant to the sector, in combination with terms referring to the industry sector. Databases that were utilised included Oshrom, Web of Science, OshUpdate, Healsafe, Embase, Medline, Chemical Engineering abstracts, Chemical Safety Newsbase and Toxfile. This scoping review was restricted to peer reviewed literature published in English, and papers dealing solely with animal data or toxicology were specifically not included.

The subsequent choice of articles was carried out in light of this process, not adhering to a systematic literature review methodology. Consequently, search returns were then assessed by both an occupational health expert and an occupational hygiene expert, specifically to initially identify pertinent review articles for further assessment. Non review articles were also included if they were deemed to either contribute to a better understanding of the range and type of ill health related to chemical exposure, or there were either details of measured exposures to relevant chemicals, or that exposures had been attributed by other means. In addition, if data within articles were not judged to be relevant or applicable to GB industry, these were excluded.

4. RESULTS

4.1 DEFINITION OF THE CHEMICAL SECTOR

Over the 5-year period of interest (2006/07 to 2010/11) there was a revision of the SIC codes from “SIC 2003” to “SIC 2007”, and descriptions of both are provided here for completeness. SIC 2003/2007 codes were assigned to the definition of the chemicals industry as shown in Appendix 1 Table A. UK SIC codes are divided into sections, each denoted by a letter. These sections can be uniquely identified by further breakdown into divisions (denoted by 2 digits), groups (3 digits), classes (4 digits) and subclasses (5 digits).

In order to use these SIC codes for the purposes of this project, a few assumptions were made. Industry classification data collected from THOR, and some data collected for the LFS, were only provided to 2-digits. Thus, data have been analysed at this divisional level, so that the results are comparable across all the relevant data sources identified in this project.

Due to the breadth of the SIC divisions related to “Import and storage of chemicals and petroleum products”, “Chemical storage” and “Chemical and petroleum products distribution (excluding pipelines)” it was likely that much of the data received from RIDDOR, THOR and the LFS would not be related to the chemical and downstream oil industry. Therefore, data for analysis in this project were restricted to include only records from the SIC 2003 divisions 23 “Manufacture of coke, refined petroleum products and nuclear fuel” and 24 “Manufacture of chemicals and chemical products” (corresponding to SIC 2007 divisions 19 “Manufacture of coke and refined petroleum products", 20 "Manufacture of chemicals and chemical products" and 21 "Manufacture of basic pharmaceutical products and pharmaceutical preparations").

4.2 REVIEW OF INDIVIDUAL DATA SOURCES

(i) Reporting of Injuries, Diseases and Dangerous Occurrences Regulations

Summary RIDDOR data obtained from HSE (Table 1) included the number of diseases reported over the 5-year period 2006/07 to 2010/11 in all industries and the chemical sector. Particular focus was inevitably placed on conditions due to substances and exposures as defined in RIDDOR.

A total of 9937 disease reports covering all industries were made, of which, 207 were from the chemical sector, as defined by SIC code.

Table 1 Diseases notified to HSE under RIDDOR (Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995), Schedule 3, over the period 2006/07 to 2010/11

Disease Name	Number of reports 5-year period 2006/07 to 2010/11	Average per year	Number of reports 5-year period 2006/07 to 2010/11	Average per year
	All industries		*Chemicals sector (defined by SIC code)*	
Poisonings (all substances)	41	8	0	0
Pneumoconiosis (excluding asbestosis)	15	3	0	0
Extrinsic alveolitis	13	3	0	0
Occupational asthma (all agents)	337	67	21	4
Occupational dermatitis (all agents)	1342	268	114	23
Other conditions due to substances	13	3	0	0
Other conditions not due to substances	8176	1635	72	14
All prescribed RIDDOR diseases	**9937**	**1987**	**207**	**41**

From the data it can be seen that approximately 2% of all reported diseases, 6% of all occupational asthma reports and 8% of all occupational dermatitis reports were made by the chemical sector.

Over the 5-year period 10% of reports made by the chemical sector were for occupational asthma, compared to 3% of reports made by other sectors (316/9730); the data indicated that a greater proportion of RIDDOR reports within the chemical sector arose from occupational asthma than was observed in all the other industries combined (excluding the chemical sector). It is evident from these data that occupational asthma is one of the prominent occupational health issues in the chemical sector. The nature of the data do not allow more statistical comparisons between groups.

Over the same period, 53% of reports made by the chemical sector were for occupational dermatitis, this compared to 13% of reports made by other sectors (1228/9730); the data indicated that a greater proportion of RIDDOR reports within the chemical sector arose from occupational dermatitis than was observed in all the other industries combined (excluding the chemical sector).

From the detailed records obtained from HSE, it was possible to further obtain figures for the conditions contained in the 72 disease notifications for other conditions (not due to "substances"). These are provided for completeness in Appendix 2 Table B.

Reported diseases by substance

From the detailed records obtained from HSE, the diseases of interest were "occupational asthma" and "occupational dermatitis" as they were "conditions due to substances" as listed in RIDDOR. Expert review of the detailed records made it possible to broadly group the substance(s) that had been reported to be associated with occupational asthma and occupational dermatitis (Table 2) and provided further information on possible reasons for the associations found. Some disease reports may have been attributed to more than one substance and therefore the number of diseases by agent differs to the data found in Table 1.

Table 2 Breakdown of reported attributable substance by the chemical sector to RIDDOR over the period 2006/07 to 2010/11, for occupational asthma and occupational dermatitis

Substance / Exposure	Occupational Asthma N (%)		Substance / Exposure	Occupational Dermatitis N (%)	
Enzymes	4	(15%)	Personal Protective Equipment (PPE)	32	(23%)
Soaps and detergents	3	(12%)	Pharmaceuticals	30	(22%)
			Soaps and detergents	16	(11%)
			Acrylic resins/epoxy resins/hardeners	8	(6%)
			Cosmetics & toiletries	7	(5%)
			Other chemicals NEC	6	(4%)
			Wet work	5	(4%)
			Dyes and pigments (incl. paints)	4	(3%)
			Preservatives	4	(3%)
			Rubber chemicals and materials	4	(3%)
			Enzymes	3	(2%)
			Organic solvents	3	(2%)
Other substance	14	(54%)	Other substance	9	(6%)
Unknown substance	5	(19%)	Unknown substance	10	(7%)
Total	**26**		**Total**	**141**	

It is important to emphasise that it is likely that cases of diseases that should be reported to RIDDOR are under reported. In addition, there will be variation in the nature and extent of RIDDOR reporting generally between duty holders. These issues will inevitably make generalisation of these findings more uncertain, as results are likely to be less representative of larger sector populations, or indeed entire working populations. The results presented thus provide an indication only of potential links between chemical exposures and the development of diseases.

(ii) Self-reported Work-related Illness (SWI)

Results of the analysis of the SWI data, undertaken by HSE (Table 3), included the estimated prevalence and rates of work-related illness caused, or made worse by, occupational exposures over the 5-year period 2006/07 to 2010/11. The results shown relate to selected comparison sectors, all industries and the chemical industry. The total estimated annual prevalence for illness due to occupational exposures was 1,039,000 for all industries; of which 8000 were within the chemical industry.

The average rate (point estimate per 100,000) of all ill health due to occupation was found to be 2880 within the chemical industry, compared to 3470 for all industries and 3060 for the manufacturing sector (of which the chemical industry is a part). However, the confidence intervals for these rates overlapped, and therefore no evidence of a significant difference could be found.

Table 3 Estimated prevalence and rates of all self-reported work-related illness caused or made worse by current or most recent job, by industry/occupation, for people working in the last 12 months, averaged 2006/07 - 2010/11

Industry/Occupation	Work-related illness ascribed to their current/most recent job					
	Averaged estimated prevalence (thousands)			Averaged rate per 100 000 employed in last 12 months		
	central	95% C.I.		**central**	95% C.I.	
		lower	upper		lower	Upper
Office based occupations	**3**	2	5	**2510**	1530	3490
Laboratory based occupations	*****	*	*	*****	*	*
Factory/Warehouse based occupations	**2**	1	3	**3070**	1650	4490
Other occupations	*****	*	*	*****	*	*
Chemical industry	**8**	6	10	**2880**	2160	3590
Manufacturing	**97**	90	104	**3060**	2850	3280
Agriculture, forestry and fishing	**12**	9	14	**3700**	2960	4440
Construction	**92**	85	99	**3730**	3450	4000
Human health and social work activities	**190**	180	199	**5060**	4800	5310
All Industry	**1039**	1015	1062	**3470**	3390	3550

* Sample numbers too small to provide reliable estimates Source: Labour Force Survey (LFS)

Self-reported ill health by occupation

Estimates for the chemical industry were further analysed, based on broad occupational categories; office based, laboratory based, factory/warehouse based and other occupations. Specific occupational breakdowns could not be undertaken due to small sample sizes. The average rate (point estimate per 100,000) for factory/warehouse based occupations (3070) was greater than the rate for the chemical industry overall (2880) and the manufacturing sector overall (3060). However, the confidence intervals for these rates overlapped and therefore no evidence of a significant difference could be found.

Self-reported ill health by type of ill health

From the list of illnesses that the SWI collects information on, there were two that were of particular interest: "breathing or lung problems" and "skin problems", as these might be attributable to exposures within the chemical industry.

As well as estimates for all work-related ill health, estimates were produced for musculoskeletal disorders over the 5-year period. Unfortunately, it was not possible to calculate prevalence or rates for the other ill health categories within the chemical industry (particularly respiratory or skin conditions), due to small numbers.

Additional analysis for the 7-year period 2005/06 to 2011/12 and the 9-year period 2003/04 to 2011/12

Extending the time period allowed more estimates to be produced, as more sample data were available. Estimates were thus additionally produced for laboratory-based occupations within the chemical industry for all work-related illness. However, increasing the period to cover 7 years, or 9 years, only allowed for one additional ill health category estimate to be produced for

stress, depression or anxiety. No prevalence or rates for respiratory or skin conditions could be calculated, due to small numbers.

After extending the time period to 7 years, or 9 years, the rate (per 100,000) for all work-related ill health within the chemical industry remained similar to the 5-year results obtained. The confidence intervals continued to overlap and no evidence of a significant difference could be identified between the chemical sector and the manufacturing industry sector and the all industry sector combined.

(iii) The Health and Occupation Research Network

Data obtained included estimated numbers of cases and incidence rates (per 100,000) for occupational asthma and contact dermatitis in the chemical sector (as defined by the SIC division codes from the project definition), manufacturing sector and all industries covering the period 2006 to 2010 (Table 4 and Table 5). Both these tables contain estimated numbers of cases due to the methods used by THOR (in brief, not all physicians that report to this scheme do so every month, and as a consequence an estimate of their total yearly reports are made). Estimated number of cases and incidence rates reported to THOR-GP could not be calculated due to small numbers.

These figures should be considered as conservative estimates; as they have not been adjusted to reflect missing cases due to non-participation and response rates of eligible physicians. Additionally, some of the cells were based on small numbers of actual cases and therefore subject to a random error; which may result in wide confidence intervals. No further information on confidence intervals was provided, and consequently no inferences about differences between groups could be drawn.

Table 4 Occupational asthma: Annual average estimated cases and incident rates per 100,000 employed, 2006-2010

	SWORD		OPRA	
	Annual average estimated cases	**Rate per 100,000 workers per year[a]**	**Annual average estimated cases**	**Rate per 100,000 workers per year[b]**
Manufacture of coke, refined petroleum products and nuclear fuel (SIC 2003 code 23)	5	10.2	0	0
Manufacture of chemicals and chemical products (SIC 2003 code 24)	10	3.7	5	64.9
Manufacturing	**136**	**3.7**	**28**	**29.4**
All industries	**279**	**1.0**	**83**	**7.7**

[a]Data from the Labour Force Survey (LFS), 2006-2008 used as the denominator
[b]Data from the 2005-2007 and 2008-2010 OPRA rolling denominator surveys used as the denominator

The annual estimated rate of occupational asthma for the "manufacture of coke, refined petroleum products and nuclear fuel" division of the chemical sector, as reported to SWORD, was higher than the estimated rates for both the manufacturing sector and all industries combined.

The annual estimated rate of occupational asthma for the "manufacture of chemicals and chemical products" division of the chemical sector, as reported to SWORD, was similar to the estimated rate for the manufacturing sector and higher than the estimated rate for all industries combined. The annual estimated rate, as reported to OPRA, was higher than the estimated rates for both the manufacturing sector and all industries combined.

Table 5 Occupational dermatitis: Annual average estimated cases and incident rates per 100,000 employed, 2006-2010

	EPIDERM		OPRA	
	Annual average estimated cases	**Rate per 100,000 workers per year[a]**	**Annual average estimated cases**	**Rate per 100,000 workers per year[b]**
Manufacture of coke, refined petroleum products and nuclear fuel (SIC 2003 code 23)	3	6.6	0	0
Manufacture of chemicals and chemical products (SIC 2003 code 24)	31	12.2	45	349.1
Manufacturing	**250**	**6.9**	**165**	**186.5**
All industries	**1461**	**5.0**	**439**	**41.8**

[a]Data from the Labour Force Survey (LFS), 2006-2008 used as the denominator
[b]Data from the 2005-2007 and 2008-2010 OPRA rolling denominator surveys used as the denominator

The annual estimated rate of occupational dermatitis for the "manufacture of coke, refined petroleum products and nuclear fuel" division of the chemical sector, as reported to EPIDERM, was similar to the estimated rate for the manufacturing sector and higher than the estimated rate for all industries combined.

The annual estimated rate of occupational dermatitis for the "manufacture of chemicals and chemical products" division of the chemical sector was higher than the estimated rate for both the manufacturing sector and all industries combined, as reported to EPIDERM and OPRA.

Reported diagnosis by industrial division

From the detailed records obtained it was possible to breakdown the reports made to THOR by industrial division and diagnosis category (Appendix 4 Table C). Over the 5-year period of interest for this project, 148 cases (42%) reported to THOR by the chemical sector were respiratory conditions. Of these, 63 were reports of asthma/allergy and 50 were reports of non-malignant pleural disease. Over the same period, 201 cases (57%) reported to THOR by the chemical sector were skin conditions. Of these 181 were reports of dermatitis/urticaria.

Reported diagnosis by broad occupation

From the detailed records obtained it was possible to breakdown the reports made to THOR by occupational categories; office based, laboratory based, factory/warehouse based and other occupations (Appendix 4 Table D). This breakdown was based on the broad occupational categories defined by HSE for the SWI analysis.

Overall, 251 cases (71%) reported to THOR by the chemical sector were for factory/warehouse based occupations, and of these 105 were respiratory conditions and 145 were skin conditions. A further 65 cases (18%) reported to THOR by the chemical sector were for laboratory based occupations, of these 25 were respiratory conditions and 39 were skin conditions.

Reported diagnosis by substance

From the list of illnesses that were reported to THOR, the main diagnoses of interest were "asthma/allergy" and "dermatitis/urticaria", as these might be attributed to substance exposure within the chemical sector. From the expert review of the detailed records (AA) it was possible to broadly group the substance(s) that had been reported to be associated with "asthma/allergy"

and “dermatitis/urticaria” (Table 6). Some reports of ill health may have been attributed to more than one causative substance or exposure.

Table 6 Breakdown of reported attributable substance to THOR within the chemical sector over the period 2006 to 2010, for asthma and dermatitis

Substance / Exposure	Asthma / Allergy N (%)		Substance / Exposure	Dermatitis / Urticaria N (%)	
Other chemicals NEC	11	(16%)	Pharmaceuticals	47	(21%)
Isocyanates	8	(12%)	Other chemicals NEC	27	(12%)
Aldehydes	6	(9%)	Soaps and detergents	23	(10%)
Enzymes	6	(9%)	Acrylic resins/epoxy resins/hardeners	16	(7%)
Laboratory animals and sewerage	5	(7%)	Preservatives	14	(6%)
Pharmaceuticals	5	(7%)	Personal Protective Equipment (PPE)	13	(6%)
Soaps and detergents	5	(7%)	Rubber chemicals and materials	13	(6%)
Dyes and pigments (incl paints)	4	(6%)	Metals and compounds	12	(5%)
Metals and compounds	4	(6%)	Wet work	8	(4%)
			Cosmetics & toiletries	7	(3%)
			Organic solvents	6	(3%)
			Dyes and pigments (incl. paints)	5	(2%)
			Aldehydes	4	(2%)
			Isocyanates	4	(2%)
			Petroleum oils (unspecified oils)	3	(1%)
			Plants	3	(1%)
Other/unknown substance	15	(22%)	Other/unknown substance	19	(8%)
Total	**69**		**Total**	**224**	

Due to the nature of the reporting process to THOR, it is important to emphasise that the results presented here are only able to provide an indication of potential links between substance exposure and ill health diagnosis. In particular, statistical approaches have been largely avoided given the uncertainties about numerator and denominator accuracy as applied to GB in general.

(iv) Cancer Burden Project

The Cancer Burden Project used industrial categories that were predominantly determined by CAREX (The CARcinogen EXposure Database). The following four industry sectors from CAREX were chosen as they related to the chemical sector definition being used in this project:

- Manufacture of coke, refined petroleum products and nuclear fuel
  - Petroleum refineries
  - Manufacture of miscellaneous products of petroleum and coal
- Manufacture of chemicals and chemical products
  - Manufacture of industrial chemicals
  - Manufacture of other chemical products

CAREX also provided an estimate of the numbers of the GB population ever exposed to a particular carcinogen by industry sector. These estimates were used in the calculation of attributable fractions. Further details on the methodology used in the Cancer Burden Project can be found in the Cancer Burden Methodology report[8] produced by HSE.

Cancer Registrations and Deaths

Results were based on the estimated number of cancer registrations in 2004 and cancer deaths in 2005 that could be attributed to historical occupational exposures. As cancer is, in general terms, a disease process with a significant latency, registrations and deaths in 2004 and 2005 that could be attributed to an occupational cause would have related to exposures in a few decades prior to these dates.

The CAREX industries included in the cancer burden project were ranked for both attributable registrations and attributable deaths. The estimated total number of cancer registrations in 2004 and cancer deaths in 2005 that could be attributable to historical occupational exposure in the chemical sector can be found in Table 7.

The difference between the numbers of attributable registrations and attributable deaths reflect the varying survival rates, with estimated registration and mortality numbers being similar for cancers with poor survival. Overall, there were an estimated 282 cancer registrations and 239 cancer deaths attributable to historical occupational exposure within the chemical sector.

Table 7 Number of estimated attributable cancer registrations (2004) and deaths (2005) and overall rank, by CAREX industry

Industry	Attributable registrations	Rank	Attributable deaths	Rank
Petroleum refineries	46	33	36	28
Manufacture of miscellaneous products of petroleum and coal	1	58	1	58
Manufacture of industrial chemicals	116	19	99	14
Manufacture of other chemical products	119	18	103	13
Total in chemical sector	**282**		**239**	
Total in all CAREX industries	**13598**		**8010**	
(95% Confidence Interval)	(9303, 20206)		(6888, 9977)	

Cancers and agents of interest

From the detailed results it was possible to obtain estimated attributable fractions, estimated numbers of cancer registrations and cancer deaths attributable to historical occupational exposure, for the four CAREX industries of interest, by type of cancer and agent (these data are shown in Appendix 5 Table E and Table F). The cancer burden data reinforced the fact that certain well known chemical exposures were associated with cancer development and highlighted other possible cancer/historical occupational exposure scenarios that could be worth investigating in future projects.

The largest attributable fractions across the chemical sector were found for mesothelioma and lung cancer attributable to asbestos exposure (in petroleum refineries, manufacture of industrial chemicals and manufacture of other chemical products) and laryngeal cancer attributable to exposure to strong inorganic acid mists containing sulphuric acid (in manufacture of industrial chemicals and manufacture of other chemical products).

After these, sino-nasal cancer attributable to wood dust exposure (in the manufacture of industrial chemicals and manufacture of other chemical products), soft tissue sarcoma attributable to TCDD exposure (in the manufacture of industrial chemicals) and liver cancer

attributable to exposure to vinyl chloride (in the manufacture of industrial chemicals and manufacture of other chemical products) had the largest attributable fractions.

As well as these cancer/agent combinations, the highest estimated numbers of attributable cancer registrations and deaths were for lung cancer attributable to exposure to strong inorganic acid mists (containing sulphuric acid) and exposure to cobalt.

In addition to displaying the relevant chemical sector data, the original peer reviewed papers previously cited in the cancer burden project have been summarised below for each of the following cancer/occupational exposure categories, given their relevance to currently exposed chemical workers.

- Strong inorganic acid mists and laryngeal cancer
- Strong inorganic acid mists and lung cancer
- Vinyl chloride and liver cancer
- Cobalt and lung cancer

For each category, risk estimates for the development of the cancer type were extracted not just from the paper chosen to base the cancer burden estimates on, but also from all papers considered by the relevant HSE Cancer Burden Research Reports. This allowed for a more general appreciation of the variation in the risk estimates identified within the Cancer Burden Project.

The results from these papers were then combined into a separate figure for each category. These figures detail: (a) which results were ultimately chosen to calculate the attributable numbers and (b) the variability / similarity between the various estimates of risk. *A priori*, it would be anticipated that the risk estimates from the individual papers would vary, given that each paper studied differing populations, used different methods of exposure attribution, and analysis methods, particularly in relation to the handling of potential confounders, such as tobacco smoking and alcohol consumption.

Strong inorganic acid mists containing sulphuric acid and laryngeal cancer[9]

Varying estimates were obtained in the five studies taken forward in the literature review (Figure 1; Appendix 5 Table G).

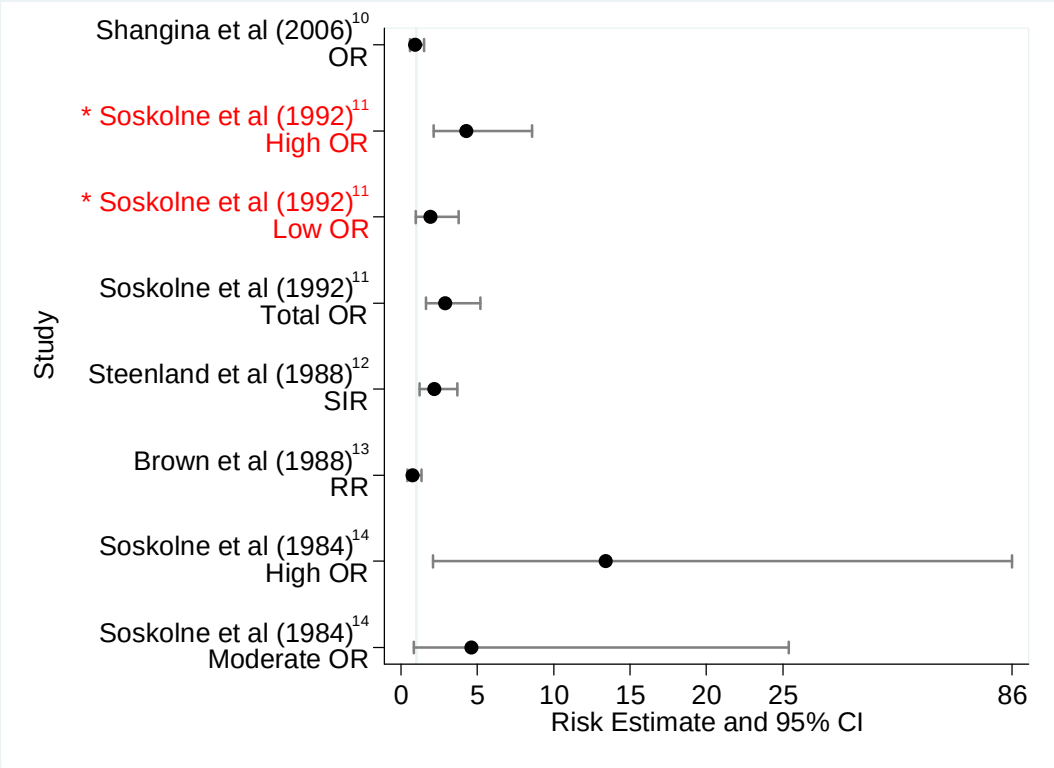

Figure 1 Laryngeal cancer: studies and estimates considered from the literature review for exposure to strong inorganic acid mists containing sulphuric acid [* (Red text) indicates the estimates chosen by the cancer burden study team]

Strong inorganic acid mists containing sulphuric acid and lung cancer[15]

Similar estimates were obtained in the three studies taken forward in the literature review (Figure 2; Appendix 5 Table G)

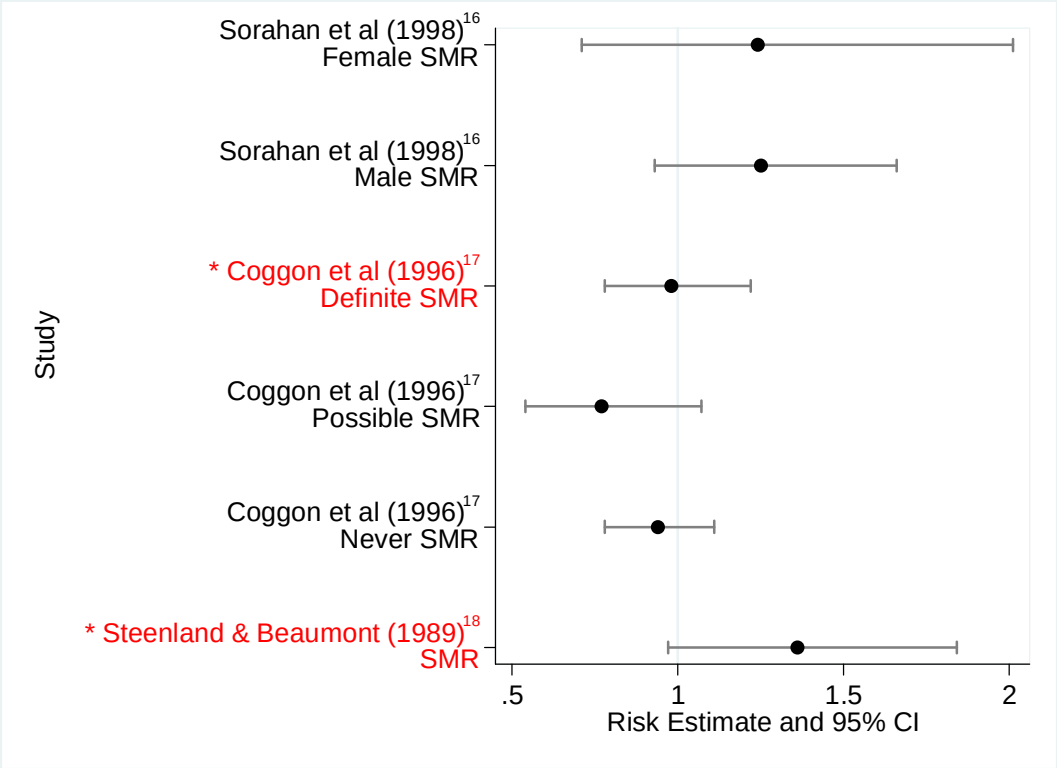

Figure 2 Lung cancer: studies and estimates considered from the literature review for exposure to strong inorganic acid mists containing sulphuric acid [* (Red text) indicates the estimates chosen by the cancer burden study team]

Vinyl chloride and liver cancer[19]

Varying estimates were obtained in the seven studies taken forward in the literature review (Figure 3; Appendix 5 Table H)

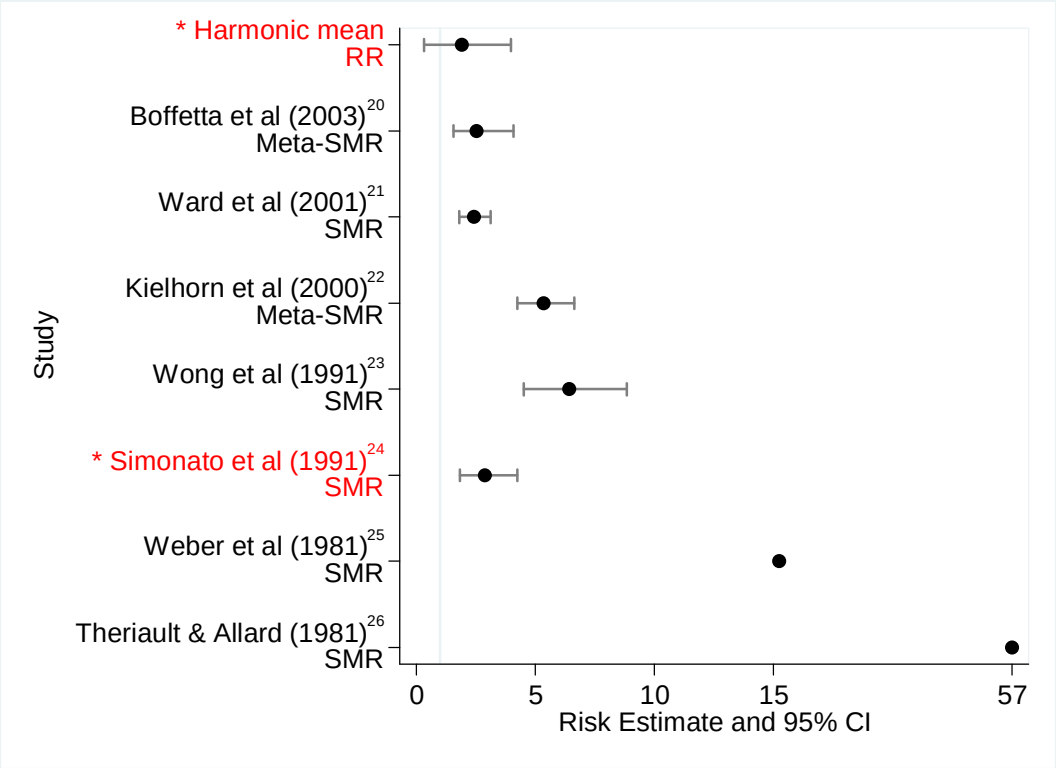

Figure 3 Liver cancers: studies and estimates considered from the literature review for exposure to vinyl chloride [* (Red text) indicates the estimates chosen by the cancer burden study team; due to the absence of specific dose-response data in any of these studies used by the Cancer Burden Project, a harmonic mean was estimated for the low exposure category]

Cobalt and lung cancer[15]

Similar estimates were obtained in the four studies taken forward in the literature review (Figure 4; Appendix 5 Table I).

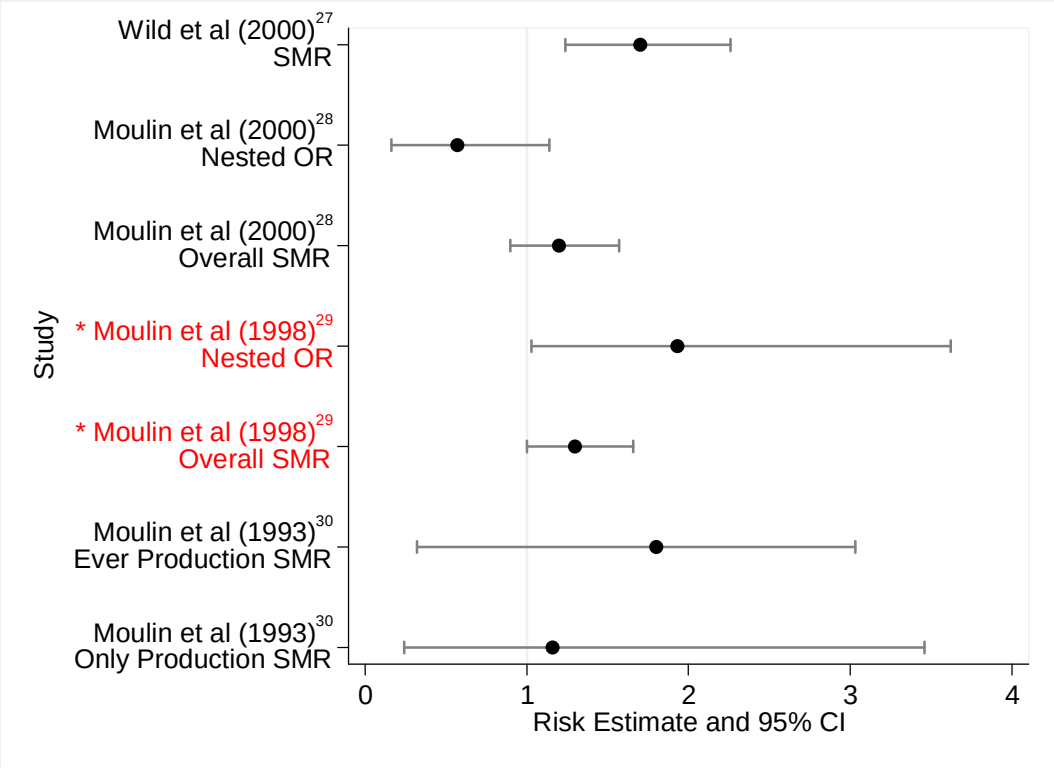

Figure 4 Lung cancer: studies and estimates considered from the literature review for exposure to cobalt [* (Red text) indicates the estimates chosen by the cancer burden study team]

(v) Occupational Health Decennial Supplement

The OHDS series provided risk estimates of various causes of mortality stratified by occupation. From the job groups included in the supplements, the following were considered relevant: “Chemical engineers and scientists” and “Chemical workers”, with respect to the two divisions “manufacture of coke, refined petroleum products and nuclear fuel” and “manufacture of chemicals and chemical products”.

Chemical engineers and scientists

In the 1995 occupational health decennial supplement, the greatest mortality risk for men was from cancer of the pleura (PMR=238, 95% CI=127-406, 13 deaths). The greatest cancer risk for men was from chronic lymphatic leukaemia (PRR=270, 95% CI=109-557, 7 registrations). There were no significantly elevated mortality or cancer risks for women (Appendix 6 Table J).

In the 2009 update of occupational mortality, a significant excess mortality risk of cancer of the pleura remained for men (PMR=190, 95% CI=104-319, 14 deaths).

From the supplementary tables available on the ONS website, it was possible to produce estimates for each cause of disease for this group for the full age range 16-74 years. In addition to cancer of the pleura, an increased mortality risk for meningeal tumour (PMR=351, 95% CI=129-764, 6 deaths) and multiple sclerosis (PMR=194, 95% CI=103-332, 13 deaths) was found for men. In women there were increased mortality risks identified for peripheral vascular disease (PMR=863, 95% CI=178-2523, 3 deaths) and cancer of the rectum (PMR=463, 95% CI=170-1008, 6 deaths), (Appendix 6 Table K).

Chemical workers

In the 1995 occupational health decennial supplement, there was a high death rate from pleural cancer for both men (PMR=159, 95% CI=113-217, 39 deaths) and women (PMR=498, 95% CI=136-1275, 4 deaths). The greatest mortality risk for men was from poisoning by “other gases” (PMR=1093, 95% CI=298-2798, 4 deaths). There were also high mortality risks for death due to injury from accidents involving explosive materials (PMR=797, 95% CI=412-1392, 12 deaths), hot substances (PMR=559, 95% CI=182-1305, 5 deaths) and machinery (PMR=199, 95% CI=125-302, 22 deaths). The greatest cancer risk for men was from cancer of the pleura (PRR=169, 95% CI=114-242, 30 registrations). For women, there was an increased risk for all leukaemia (PRR=305, 95% CI=181-483, 18 registrations) and for stomach cancer (PRR=185, 95% CI=126-263, 31 registrations) (Appendix 6 Table L).

In the 2009 update of occupational mortality, a significant excess mortality risk of urothelial cancer was reported for men (PMR=124, 95% CI=103-148, 123 deaths) and an excess mortality risk of ischaemic heart disease was reported for women (PMR=116, 95% CI=100-134, 192 deaths). The mortality risk for cancer of the pleura was no longer elevated in men (PMR=65, 95% CI=34-114, 12 deaths) or statistically elevated in women (PMR=150, 95% CI=4-837, 1 death). The high mortality risk from accidents possibly related to work in men (aged 16-64 years) remained (although not significantly) for injuries due to explosive materials (PMR 1370, 35-7650, 1 death), poisonings by “other gases” (PMR=471, 12-26350, 1 death) and hot substances (PMR 319, 8-1780, 1 death).

From the supplementary tables available on the ONS website, it was possible to produce estimates for each cause of disease for this group for the full age range 16-74 years. In addition to urothelial cancer, an increased mortality risk for cancer of the stomach (PMR=121, 95%

CI=105-138, 218 deaths) and ischaemic heart disease (PMR=106, 95% CI=102-110, 2682 deaths) was found for men. In women an increased mortality risk for hypertensive disease (PMR=221, 95% CI=111-396, 11 deaths) was identified (Appendix 6 Table M).

(vi) National Exposure Data Base

The focus of the NEDB enquiry was specifically restricted to cobalt, sulphuric acid and vinyl chloride, because these specific exposures were highlighted in other data sources as potentially important causes of ill health within the chemical sector. A search for all exposure data in the chemical sector over the period of review was also made.

Cobalt

Certain forms of cobalt (cobalt dichloride and cobalt sulphate) are known carcinogens, and in addition cobalt is a known sensitiser; that is, it is capable of causing allergic sensitisation and related diseases such as asthma.

The search of the NEDB for cobalt exposure information yielded no data for the period 2006 – 2011 in the chemical sector. There were, however, 11 data points from a single visit to a workplace, which was carried out in 2005. The results identified for this visit from the NEDB are shown in Table 8.

Table 8 Inhalation exposure data for cobalt from a single manufacturing plant in SIC: Manufacture of Other Inorganic Basic Chemicals (SIC 24.13)

Job Name	Sample type	Result mg/m^3	8 hour time weighted average mg/m^3
Bagging operator	PL	0.900000	0.840000
Static: at mixer	SL	0.370000	n/a
Static drier	SL	0.310000	n/a
Drier	PL	0.520000	0.490000
Static: at mixer	SL	0.040000	n/a
Operator general)	PL	1.650000	1.550000
Packing	PL	0.120000	n/a
Static: at mixer	SL	0.270000	n/a
Static: at mixer	SL	0.370000	n/a
Production operator	PL	0.040000	0.040000
Bagging operator	PL	0.200000	0.170000

PL=long term (8hr) personal sample. SL=long term (8hr) static sample

The workplace exposure limit (WEL) for cobalt is currently $0.1mg/m^3$. Four out of the five 8 hour time weighted average (TWA) personal exposure values were greater than the WEL but it should be noted that this data is limited to one site and the form of cobalt present at this particular site was not established.

Sulphuric acid

Sulphuric acid exposure has been highlighted as a potential contributor to laryngeal and lung cancer. The search of the NEDB for sulphuric acid mist exposure information in the chemicals sector yielded no data.

Vinyl Chloride

The search of the NEDB for vinyl chloride exposure information in the chemicals sector yielded no data.

All substances recorded in the Chemical Sector

Searches on all 13 chemical sector industries, for all substances recorded on NEDB (from 2006 to 2011) yielded 64 raw data points. This included exposure data on the following substances: azodicarbonamide, total chromium, chromium VI, gluteraldehyde, hydrazine, total isocyanates, a specific isocyanate (methylene bisphenyl di-isocyantate (MDI)), trichloroethylene, unspecified process dust and xylene. Each substance was collected from one site on one day; that is, no substance had data from more than one site.

Of the 64 raw data points, 25 were 8-hour TWA values calculated from both long and short-term personal exposure samples. The 8-Hour TWA values were compared to relevant workplace exposure limits; this is summarised in Table 9. Of the nine substances reviewed, only one 8-Hour TWA (azodicarbonamide from the mixing of chemicals for wholesale) was above the WEL. No further analysis of these data was possible, particularly as no contextual information was associated with it. The small size of the data set demonstrated the paucity of exposure data in the chemical sector for this time period.

Table 9 Summary of exposure data from NEDB for all substances for all chemical sector

Substance & WEL (8hr TWA)	Industry	Process	Jobs	Number of 8hr TWA results	Range mg/m^3	%>WEL
Azodicarbonamide (1mg/m^3)	Wholesale of chemical products	Chemical Mixing	Mixing of chemicals inc blending and batching	1	n/a	100 (~3x)
Total chromium (0.5mg/m^3)	Basic industrial chemicals manufacture	Chromic acid plant	Loading vessel Cleaning, Process worker	4	0.001 – 0.008	0
Chromium VI (0.05mg/m^3)	Basic industrial chemicals manufacture	Chromic acid plant	Loading vessel Cleaning, Process worker	4	0.0004-0.003	0
Gluteraldehyde (0.2mg/m^3)	Basic industrial chemicals manufacture	Chemicals production	Chemical transfer	5	0.001-0.013	0
Hydrazine (0.03mg/m^3)	Specialised chemical products manufacture	Reactor Loading	Topping up reactor	1	n/a	0
Methylene bisphenyl di-isocyantate (MDI) (0.02mg/m^3)	Basic industrial chemicals manufacture	Resin production	Plant operator	6	0.00005-0.0009	0
Unspecified process dust (10mg/m^3)*	Wholesale of chemical products	Chemical mixing	Mixing of chemicals including blending& batching	1	n/a	0
					Range ppm	
Xylene (50ppm)	Basic industrial chemicals manufacture	Road tanker unloading	Outer wrap operator	1	n/a	0
Trichloroethylene (100ppm)	Wholesale of chemical products	Drum filling	Drum filling	2	both 0.5	0

*not a WEL, but level at which, when present in air at equal to or greater than 10mg/m^3 (for inhalable), can become a substance hazardous to health in accordance with the COSHH regulations (2002) as amended.

(vii) Industry Data

The type and availability of industry data relating to ill health and exposures was discussed with one industry representative (CIA). The CIA collects statistics on RIDDOR, reportable disease incidents and occupational illnesses for each member site (the latter includes both RIDDOR and non-RIDDOR reportable incidents). The occupational illnesses for which data are recorded are shown in Table 10.

Table 10 CIA Occupational Illness data collected

Chemical agents	**Physical agents**	**Biological agents**	**Other (not due to chemical, physical or biological agents)**
• Respiratory illnesses Includes:- - Work-related rhinitis - Occupational asthma - Other lung disorders • Skin illnesses Includes:- - Contact Urticaria - Irritant Contact Dermatitis - Allergic contact dermatitis • Cancer and Malignant Blood Disease • Other illnesses	• Upper limb disorders • Neck problems • Back problems • Lower limb • Occupational hearing loss • Other illnesses	• Diseases contracted whilst travelling on business e.g. malaria • Allergies due to exposure to biological agents • Other illnesses	• Work-related stress • Other illnesses

4.3 REVIEW OF PEER REVIEWED LITERATURE

Applying the search strategy, as defined by the search terms, identified 453 articles either by title or by abstract (see Appendix 8).

Review articles that comprehensively covered the topic of interest were not identified using the pre-defined search strategy, although certain reviews that dealt with some specific aspects were identified, as were a number of articles pertinent to the main focus of this project. Consequently, a mix of reviews and original articles have been reviewed below, with particular relevance to ill health associated with chemical sector exposures, and also to specific occupations or tasks associated with the development of ill health. All reviewed articles were written in English, and *a priori* any papers dealing with predominantly toxicological issues or biological effects only were not chosen for review.

By its very nature, this review was not comprehensive; its inclusion here is intended to complement the findings of the data sources interrogated in relation to ill health and chemical exposure, to assess if the recent literature is broadly consistent with the former, or raised other issues that were not identified.

Specific disease endpoints identified in this review that will be expanded upon below are cancers, airways disease including asthma, neurological, dermatological and a group of miscellaneous conditions. Where papers within reviews are discussed, only the comments within the review are included here. A further separate review of the additional cited paper was not undertaken.

From the specific standpoint of job tasks and exposures identified by the review, the following areas will be covered; general comments about exposures across sectors and specific comments about exposure to benzidine, diacetyl, products of rubber manufacturing and metals and metal processing. Brief comments will also be made concerning future risks associated with chemical exposures.

4.3.1 SPECIFIC DISEASES

Cancers

Bladder cancer: over 200 chemicals, with varying strengths of evidence, were identified to be potentially associated with bladder cancer development in a recent review (Declos and Lerner (2008)[31]. This work noted that of these agents, the most well established association was for the aromatic amines, and specifically β-Naphthylamine, 4-aminobiphenyl and benzidine. It is pertinent that the International Agency for Research on Cancer (IARC) has classified eleven specific aromatic amines as group 1 (definite), group 2A (probable), or group 2B (possible) human carcinogens, and also lists magenta and auramine manufacturing as a group 1 exposure circumstance, with petroleum refining and petrochemical manufacture as a group 2A exposure circumstance.

This review also noted that there was a potential genetic component identified by Vineis *et al* (1994)[32] that potentially dictates the susceptibility to urinary carcinogens. Whilst not reviewed in depth here, individuals with NAT2 genotype, affecting N-acetylation, may have an increased risk of bladder cancer.

Other urological malignancies: in relation to renal cancer, Golka et al (2004)[33] identified an approximate eight fold risk of renal cancer in workers who were highly exposed to trichloroethylene in a cardboard factory, with frequent symptoms of acute intoxication. Further support of a link from two case control studies was also cited in this review[34 and 35]. These findings conflicted with other data cited within the same review[33]. For example, a Swedish study[36] did not identify elevated risks for renal cell cancer where inhaled exposures were controlled to ≤ 20ppm. The related chemical perchloroethylene was also summarised as having conflicting evidence for renal carcinogenicity[33]. In relation specifically to other urological cancers, it was summarised that the risk due to occupational exposure appears to be negligible for prostate cancer and that no relevant studies on occupational factors were found for testicular cancer[33]. In conclusion, Golka *et al* drew attention to the fact that the urological malignancies reviewed had a generally favourable prognosis when compared with other malignancies, and as a consequence mortality studies were likely to underestimate risks associated with occupational exposures.

Cancer and pharmaceutical work: data from seven studies relating to pharmaceutical workers identified by Heron and Pickering (2003)[37] focussed on cancer incidence, with elevated risks identified for breast cancer in two relevant studies shown. The authors concluded overall that apart from a group of workers exposed to sex hormones "before modern methods of exposure control had become widely established, no significant exposure-related excess morbidity or mortality" had "been identified in workers in the pharmaceutical industry".

The same review[37] also discussed dermal exposures to cytotoxic anti-cancer drug exposures for workers manufacturing and developing these products. It was noted that biological effects could be anticipated at very low levels of absorption. No ill health or disease endpoints were discussed.

Airways disease including asthma

At a population level, Baur and Latza (2005)[38] reviewed claims in the year 2003 to both the German Ministry of Labour and Social Affairs, and to the Federation of Statutory Accident Insurance Institutions. Within the category "obstructive airways diseases due to allergens" chemical workers were ranked 6th highest; with 23 of the 922 cases (2.5%). Specifically in relation to the chemical industry, 19 of the 181 cases (10.5%) were reports from chemical workers for the category "obstructive airway diseases due to irritants and toxic agents" and 23.6% of cases of "isocyanate-induced diseases" were reported in chemical workers.

In terms of sensitisation and asthma, Heron and Pickering (2003)[37] identified exposure to certain antibiotics: in particular penicillins and cephalosporins, in addition to enzymes in pharmaceutical manufacturing sector as risk factors. Additionally, the active pharmaceutical ingredients cimetidine, lisinopril, α-methyldopa and salbutamol were recognised as being associated with respiratory problems, although perhaps through a direct chemical rather than immune mechanism.

Airway responses to inhaled opiates were also highlighted by this review[37], and a discussion of putative mechanisms was included, indicating this observed effect may be due to at least a combination of direct histamine release and antibody mediated effects.

Occupational asthma was also discussed by Fairhurst (2003)[39], particularly in the context of available clinical and research data. The authors identified that to date knowledge in this area is almost entirely reliant on human observational data, with a general lack of appropriate and reliable experimental toxicology data.

Neurological conditions

Morata (2003)[40] discussed the issues identified in a NIOSH convened workshop to investigate the combined effects of chemicals and noise on hearing, given the current practice to base hearing protection programmes on exposures to noise alone; assuming that this is the single relevant workplace exposure. The review identified that, although noise is particularly damaging to the cochlea, industrial chemicals tend to affect both the cochlear structures and the central nervous system. As a consequence, the need for mechanistic research was highlighted to identify the ways in which chemicals may damage hearing, the responses of different animal species, the interactions between chemicals, and the physical and endogenous factors that may also be relevant in relation to hearing loss.

More recently, Morata and Johnson (2012)[41] reviewed the evidence for the ototoxic effects of specific chemicals. It was considered that human data were consistent with the evidence from animal studies, supporting the fact that toluene, styrene and solvent mixtures are potentially ototoxic. The authors concluded that the effect on audiometry caused by certain chemicals could be the same as those seen in noise induced hearing loss on high frequencies, but in addition other frequencies could also be affected. The review also identified difficulties with current research approaches, and in particular the difficulty in human studies of obtaining reliable exposure data for both chemicals and noise.

Morata and Johnson (2012)[41] also discussed carbon monoxide poisoning. They noted that acute exposures to this gas, without any concomitant noise exposure, could induce auditory damage, with an associated abnormality in the extended high-frequency region of the audiogram. Similarly, lead exposure was discussed in relation to hearing loss. Previous work was cited to confirm an association between lead exposure and central auditory effects. Previous studies of lead exposure in children were also discussed in the context of ototoxic effects. It was concluded that whilst the extent and nature of chemicals, for which human ototoxicity data are available, is small; styrene, toluene, lead and carbon monoxide have been the most extensively studied.

In terms of chemical exposures and neuro-developmental problems, Julvez and Grandjean (2009)[42] identified 15 papers addressing these issues specifically relating to pregnancy. This review discussed general issues, including limitations of study design and exposure estimation, and also that of the 201 industrial chemicals known to be neurotoxic to humans, only five (arsenic, lead, methylmercury, toluene, and PCBs) were regarded as potential causes of human neuro-developmental toxicity.

Additionally, Fairhurst (2003)[39] also discussed Chronic Toxic Encephalopathy, a condition potentially related to long term organic solvent exposure, typified by fatigue, irritability, apathy, poor memory, concentration difficulties, personality change and depression. The pathophysiology that underlies the condition was not thought to be well understood.

Dermatological conditions

Mehlman (2006)[43] performed a review of the evidence for a link between malignant melanoma and exposures to chemicals in the oil refining and chemical industries. This was not a systematic review, and no strength of evidence was attributed to the included papers. A table of 12 studies published between 1976 and 2004, which found an increased risk for malignant melanoma at specific petrochemical and refinery sites, was presented with the associated relative risks ranging between 1.1 to 6.7. A further table cited 14 studies showing an increased risk of malignant melanoma in oil refinery workers, with relative risks ranging 2.4 to 6.7. The review did not produce a meta-analysis, and did not discuss negative studies. No further

conclusions can reasonably be drawn from these data given the non-systematic nature of the review.

In relation to dermatological problems, the previously discussed review by Heron and Pickering (2003)[37] identified various examples of skin sensitisation within the pharmaceutical sector including being caused by ranitidine, cimetidine, proton pump inhibitors and a range of cytotoxic agents including mechlorethamine, nitrogen mustard, mitomycin C, carmustine, melphalan and chlorambucil. Exposure to corticosteroids had been have found by several studies to cause work-related adverse effects, including acne and erythema.

Miscellaneous conditions

Heron and Pickering (2003)[37] noted that acute toxicity from pharmaceutical products was found to be rarely reported in the published literature, although reports included a case of hypoglycaemic coma due to glibenclamide exposure, and another of barbiturate toxicity amongst several operators. In addition, a case of severe health effects from chronic exposure to vitamin D3 was also cited.

It was also identified within the review[37] that the sex hormones oestrogen and progestagens were documented in several now highly historic studies to have caused gynaecomastia (swelling of the breast tissue), galactorrhoea (milk production from the breast), psychological effects, testicular discomfort and loss of libido in male workers. In female workers menstrual disorders were also discussed.

Finally, Heron and Pickering summarised that occupational exposure to corticosteroids was potentially associated with a reduction in human corticotrophins, and an abnormal synacthen test result, in a small proportion (2 of 12) workers involved in the manufacture of betamethasone[37]. Occupational exposure to steroids was also described as causing systemic effects, including hypertension and effects suggestive of Cushing's syndrome.

4.3.2 DISEASE ATTRIBUTABLE TO WORKPLACE EXPOSURES

The majority of the papers identified in this process related to either a single substance or exposure, or a group of substances commonly used together. Ordinarily, the papers also focussed on a particular industrial sector, although there were certain exceptions where exposures to a particular substance were described in all the key industries using that substance.

General exposures across sectors

Hauser and Calafat (2005)[44] summarised the relationship between human health and exposure to phthalates. This review assessed human health in its wider sense, including both occupational and environmental exposures to these agents. The authors described the wide spectrum of industrial applications of high molecular weight phthalates (primarily used as a plasticizer in the manufacture of flexible vinyl) and low molecular weight phthalates (used in personal care products and as plasticizers for cellulose acetate), the metabolism of phthalates, and the studies on health effects of phthalates in human populations. This comprehensive review identified certain potential ill health consequences of exposure (including male reproductive tract development, male and female reproductive function and asthma / obstructive airway disease) but concluded that "depending on the health endpoint of interest, there is currently only limited or inadequate human data on the relationships between exposure to phthalates and human ill health effects".

Single substance or mixed exposure in a single sector

Benzidine: Brown et al (2011)[45] described a historical cohort study of 997 workers assessing cancer incidence and mortality among workers exposed to benzidine at a chemical production facility. This paper reported that their results supported previous findings of an increased risk of bladder cancer among individuals exposed to benzidine and other arylamines.

Diacetyl: a cross sectional study by van Rooy et al (2009)[46] assessed lung function and respiratory symptoms initially among four chemical workers producing diacetyl (2,3-butanedione) for food flavourings. The investigation of these cases led to the development of an historical cohort study of a further 175 workers at the same workplace. The cohort study assessed exposures, respiratory symptoms, lung function and exposure-response relationships in workers having worked at the relevant plant between 1960 and 2003. A relationship between exposure and a measure of lung function, the FEV_1, was observed, suggesting that diacetyl production posed an occupational hazard associated with risks of developing lung disease. This process is characterised and understood to relate to a bronchiolitis obliterans type illness.

Rubber and rubber goods manufacturing: Hanley et al (2012)[47] undertook an update of a retrospective cancer incidence and mortality study in a rubber chemical manufacturing plant. Workers had been exposed to o-toluidine, aniline, and nitrobenzene in a rubber chemical manufacturing plant from 1976-2004. The authors commented that breathing zone air sampling data were well below published occupational exposure limits for these chemicals, but additional cases of bladder cancer had been reported.

Macaluso et al (2004)[48] retrospectively characterised exposure (from the 1960s to 1980s) to 1,3-butadiene, styrene, and dimethyldithiocarbamate among synthetic rubber workers. The authors identified difficulties with estimating agent-specific effects, and highlighted the limitations of their methodology; including the lack of adequate industrial hygiene data to validate these estimates.

De Vocht et al (2009)[49] reviewed exposures to aromatic amines and inhalable aerosols in rubber tyre manufacturing in Poland. Quantified exposures to inhalable aerosols and aromatic amines were estimated using a company specific job exposure matrix (JEM). Cancer risks associated with cumulative exposures were calculated following adjustment for co-exposures, gender and year of birth. It was identified that exposure levels were higher for women than for men, and also that aromatic amine exposure was significantly associated with increased urinary bladder cancer risk (RR = 7.32-8.27), depending on exposure level, and prostate cancer at low levels only (RR = 5.86).

In women, increased risks were found for all cancers (RR = 2.50) and for cancers of the digestive organs and peritoneum (RR = 4.54) at low levels of aromatic amines and aerosols only, whilst an exposure-response association with breast cancer risk was found[49].

Inhalable aerosol exposure was associated with cancers of the liver and intrahepatic bile ducts in a dose-dependent manner, while dose-dependent reduced risks were found for respiratory cancers (most notably the larynx) and cancer of the colon[49]. The authors concluded that increased risks for specific cancer sites in this rubber plant were similar to Western Europe and the US. However, several cancer risks were gender-specific, which could have related to higher exposure levels in women or to differences in exposures to chemicals not assessed in this study.

Metals processing: two papers assessed beryllium exposure at plants in the US, Schubauer Berigan (2011)[50] and Thomas et al (2009)[51]. The former described the results of a cohort mortality study of workers at seven beryllium-processing plants. The authors concluded that

their findings reaffirm that lung cancer and chronic beryllium disease (CBD), and suggest that chronic obstructive pulmonary disease (COPD) and nervous system and urinary tract cancers, are related to beryllium exposure. Cigarette smoking and exposure to other lung carcinogens are unlikely to explain these elevations. Thomas et al (2009)[51] described the efficacy of a programme to prevent beryllium sensitisation among new workers at a copper-beryllium alloy processing facility; in 2000, the facility began testing newly employed workers with beryllium lymphocyte proliferation tests (BeLPTs) at first employment and at intervals during employment. They compared sensitization incidence rates (IRs) and prevalence rates for workers hired before the program (legacy workers) with rates for new workers. They concluded that fewer workers became sensitized after implementation of the preventive program. However, the low statistical power, due to the facility's small workforce prevented a definitive conclusion about the program's efficacy.

Additionally, Park et al (2009)[52] described a quantitative risk assessment for hexavalent chromium exposure and lung cancer risk in the US chromate industry. The analysis predicted that current occupational standards for hexavalent chromium permitted a lifetime excess risk of dying of lung cancer that exceeded one in ten, which was consistent with previous risk assessments.

4.3.3 FUTURE RISKS

Whilst the limited scope of this literature review precluded any comprehensive assessment of future health risks associated with chemical exposures, various were identified from the reviewed literature.

Specifically, Brun (2009)[53] produced a report for the European Agency for Safety and Health at Work relating to emerging chemical risks related to occupational safety and health. This consisted of the results from a Delphi survey. The main identified emergent risks to health were categorised into three groups: these were (i) particles (nanoparticles, ultra-fine particles and man-made mineral fibres), (ii) allergenic and sensitising agents (including epoxy resins, isocyanates and dermal exposures) and (iii) carcinogens, mutagens and reprotoxic substances (including asbestos, silica, wood dust, organic solvents, endocrine disruptors, organic pollutants, aromatic amines, biocides, azo-dyes, and combined carcinogen exposures). It is evident that certain of these risks already exist in workplaces.

The author also included comments about sector specific risks (and highlighted the construction and waste treatment sectors as important here, given the nature of certain exposures including VOCs, lead, cadmium, mercury). Additional comments were also included in relation to combined risks, with particular relevance to the interface between exposures and psychosocial risks. This latter set of comments included problems specifically faced by small and medium sized enterprises and the specific problems associated with controlling risks to sub contracted workforces.

5. DISCUSSION

The main aims of this project were three fold. The first was to develop a working definition of the chemical sector, and this was achieved successfully by utilising a descriptive definition already developed by HSE. SIC codes were applied to these descriptive terms and are listed in full in Appendix 1. The formulated listing of SIC codes was then applied to other components of this work, described in this report. This allowed a common approach to identifying data that may relate specifically to ill health in this sector. This listing will now be available to other interested parties who wish to carry out similar or related future work.

The second aim of this project was to review and critically appraise the data sources of reported ill health and related exposure data in the chemical sector. The project team set out *a priori* to identify potential useful sources of such data, and seven specific sources were identified and developed. In general terms identification of the source and obtaining data was relatively straightforward.

In more specific terms, seven sources of data were utilised for the purposes of assessing up to date levels and types of illness seen in the chemical sector.

(i) Reporting of Injuries, Diseases and Dangerous Occurrences Regulations

RIDDOR data that were able to be accessed were useful in this regard. Whilst it is acknowledged that there are some limitations to this data due to under-reporting there is still much useful information within the dataset. The data identified that a variety of illnesses attributed to occupational exposures were reported in the relevant sector. In particular, occupational asthma and occupational dermatitis were highlighted. The overall pattern of RIDDOR reports differed between the chemical sector and all other sectors combined. Indeed, it might be anticipated that this would be the case, given that a high proportion of the well described and documented causes of asthma and dermatitis relate to chemicals produced in the chemical sector.

Specifically, there were 21 reports of occupational asthma (10% of all chemical sector reports for the period 2006/07 to 2010/11) and 114 reports of occupational dermatitis (55% of all chemical sector reports for the same period). This compares with the all industry reports of 3% of all reports being for occupational asthma and 14% of all reports being for occupational dermatitis. These RIDDOR data confirm that cases of asthma and dermatitis attributed to work are still being reported, and are likely to be over reported in the chemical sector in relation to all other sectors combined. A further sensitivity analysis was not performed assessing reports between other individual sectors. The increased proportion of RIDDOR reports seen may be due to a number of interconnected reasons. Whilst the sector may be responsible for more exposures that cause these conditions, it is also likely that as a consequence of this, cases are identified more readily through appropriate means including health surveillance where required. Again, as these data relate to proportions rather than incident rates, higher levels of reports for asthma and dermatitis may in part also relate to less illness in other categories. No further inference is possible from these cross sectional data in terms of levels reported in comparison to other industrial sectors.

Limited information was available on the breakdown of causes for asthma and dermatitis reported to RIDDOR and classified to the chemical sector. Of the 21 cases of occupational asthma, five were attributed to an unknown cause, but four were attributed enzyme use (three of which were also attributed to soaps and detergents) and 14 to a mixed group of individual exposures. Whilst of course it is not possible to draw firm conclusions from these additional

individual causes, these included: pathogens and micro-organisms, laboratory animals and sewerage, wood and wood dusts, isocyanates, cement, plaster and masonry, pharmaceuticals, metals and compounds, organic solvents, other chemicals, and dyes and pigments.

It is noteworthy that a high proportion of dermatitis cases reported (23%, 32 cases) mentioned personal protective equipment (PPE) as a possible contributory factor, either due to a skin reaction related to PPE use itself, inadequate provision of PPE, failure of PPE or incorrect use of PPE. In addition, 30 cases were attributed to pharmaceuticals, 16 to soaps and detergents and 10 to an unknown cause.

(ii) Self-reported Work-related Illness

Despite the reliance on self-reporting (as opposed to physician or health care professional diagnosed), data from the self-reported work-related illness component of the LFS added a different dimension to the assessment of ill health in the chemical sector. The collected information relied upon a positive answer to the question "within the last twelve months have you suffered from any illness, disability or other physical or mental problem that was caused or made worse by your job or work done in the past?" Respondents who report yes are then asked a supplementary question relating only to their "most serious illness". There are no data available for either the type or effect of work-related conditions, except those considered as the most serious, which evidently may underestimate the effect of some conditions compared with others.

Nevertheless, the reported rates for the chemical sector, 2880 cases per 100,000 employed in the last 12 months, were lower than the all industry average 3470 cases per 100,000 employed. The approximate level was maintained in a fuller, extended, analysis taking into account data from either a 7 or 9-year period.

(iii) The Health and Occupation Research Network

When considering occupational asthma, for the study period 2006 – 2010, using data from reporting respiratory physicians, the estimated incidence rate of this condition was elevated for the chemical sector in comparison to all industries. No formal tests of significance could be undertaken due to the nature of the data available. However, using the pre-defined SIC codes for the chemical sector definition used in this project the respective rates per 100,000 were approximately 10.2 and 3.7, for the two components of the chemical sector compared to 1.0 for all industries. The manufacturing sector overall also had higher levels of reported rates of occupational asthma (approximately 3.7 per 100,000) compared to the all industry rate. Although OPRA reporters (occupational physicians) did not report any cases of occupational asthma in the manufacture of coke, refined petroleum producers and nuclear fuel, data for the manufacture of chemicals and chemical products were consistent with the SWORD data.

When considering occupational dermatitis, the estimated incidence rate of this condition for the manufacture of chemicals and chemical products, as reported by dermatologists in EPIDERM, was higher than both the all industry rate and that of the manufacturing sector. The manufacture of coke, refined petroleum products and nuclear fuel had an estimated incidence rate similar to both the all industry rate and that of the manufacturing sector. Data from the OPRA scheme identified higher rates of reported dermatitis in the manufacture of chemicals and chemical products and also in the manufacturing sector overall. It is also worth noting that the all industry estimated rates were higher for occupational contact dermatitis than for occupational asthma (when SWORD was compared with EPIDERM) and additionally for the same comparison within OPRA, supporting the reporting consistency of the figures presented.

Further breakdown of the raw THOR data may assist assessment and provide context to these figures, although no statistical inference can be drawn from these cases. Within the respiratory cases reported to the THOR schemes, all cases of cancer, non-malignant pleural disease and pneumoconiosis were attributed to asbestos (except a single case of pneumoconiosis attributed to nickel and a single case of lung cancer attributed to smoking tobacco). The eight cases of inhalation accident were attributed to aldehydes, acids, sulphur dioxide and a combination of both acid and sulphur dioxide exposure.

The causes of occupational asthma in the chemical sector identified by THOR, in rank order, were isocyanates, aldehydes, enzymes, laboratory animals and sewerage, pharmaceuticals and soap and detergents. Other categories below these causes contained four or fewer reports. As well as being a cause of inhalation accidents, it is noteworthy that aldehydes appeared in the top five causes of occupational asthma/allergy. Active pharmaceuticals also appeared in the leading causes of occupational asthma/allergy, exposures that will presumably only occur in a sub-sector of the manufacture of chemicals and chemical products. Other less frequently identified causes of occupational asthma reported included two cases due to herbicide exposure and two cases due to nitrile exposure. The causes identified by THOR as relevant to the chemical sector were in general consistent with the known causes of occupational asthma[54].

The causes of occupational contact dermatitis in the chemical sector identified by THOR, in rank order, were pharmaceuticals, soaps and detergents, acrylic resins/epoxy resins/hardeners, preservatives, PPE, rubber chemicals and materials and metal compounds. Other less common categories included eight reported cases or less. Similarly to occupational asthma, a mixed group of smaller numbers of reported cases, whilst less robust in terms of a statistical interpretation, assist further the risk profile for the sector. These included five cases attributed to colophony and flux.

It is noteworthy that personal protective equipment (PPE) was identified as a contributor to the development of occupational dermatitis within the sector, consistent with the data already described in relation to RIDDOR reported cases. Furthermore, the identified rubber chemicals and materials category might well share a common origin in a number of cases, as rubber gloves used for PPE are themselves a potential cause of contact dermatitis. Similarly, wet work is often associated with repeated hand washing and the use of cosmetics and toiletries. The data do not allow any further detailed inference. Within the chemical sector, for example, the latter agents may be the relevant causative exposure for dermatitis.

Although metals and their compounds appear in the top ten causes of dermatitis for the sector, no further comment can be made about their causative role, as the details of the metals involved are not available. Within this disease category, there were only two cases of urticaria recorded; one attributed to dyes and pigments and the other to a combination of grain, dust and pharmaceuticals.

In terms of other dermatological diagnoses, a single case of skin cancer was attributed to ethylene oxide. There were 14 additional cases recorded as “other dermatoses”, although again no further diagnostic information is available. The nature of most of the implicated substances were acids, alkalis, active pharmaceuticals and pesticides.

Finally, these data triangulate well with other sources. For example, data supplied by THOR are broadly consistent with the RIDDOR derived data in terms of potential causes of ill health within the chemical sector. For example, enzymes, soaps and detergents were identified in both schemes as causes of occupational asthma and pharmaceutical agents, soaps and detergents and acrylic resins were identified as important contributors to dermatitis in both schemes.

(iv) Cancer Burden Project

Assessment of the cancer burden data with relevance to the chemical sector identified some important issues relating to historical exposures that have been implicated in current cancer causation. Overall, the cancer burden report identified that 282 of 13,598 cancer registrations, attributable to occupation in 2004, might be attributed to exposures in the chemical sector, and that 239 of 8010 cancer deaths in 2005 could also be similarly attributed. The chemical sector definition used was based on the definition developed in this project.

When considering individual cancers, chemical sector exposures were linked to 13 of the 56 attributable registrations for cancer of the larynx, and to five of the 20 attributable cancer deaths. Three exposures contributed in total: asbestos, the rubber industry and strong inorganic acid mists containing sulphuric acid; of which two were considered for the chemical sector (asbestos and strong inorganic acid mists containing sulphuric acid). For the latter agent alone, encountered in the chemical sector, 13 of 46 registrations and five of 16 deaths due to laryngeal cancer and 24 of 76 registrations and 20 of 67 deaths due to lung cancer were attributed with this exposure. Indeed, the chemical sector contributed 166 of 5,442 attributable registrations and 145 of 4,745 attributable deaths due to lung cancer overall.

More specifically in relation to lung cancer, cobalt exposure in the chemical sector was attributed as cause for 16 of 73 registrations and 14 of 63 deaths due to this condition. A single registration and death was attributed to cadmium as a cause of lung cancer in the same sector, representing one of nine lung cancer registrations and one of eight lung cancer deaths attributed to cadmium exposure.

In relation to liver cancer, two out of five cancers, for both registrations and deaths due to this condition were attributed to the chemical sector, the relevant agent being exposure to vinyl chloride. The chemical sector was associated with two of three attributable liver cancer registrations and deaths from this exposure.

In relation to pancreatic cancer, numbers were very small. Only a single case of this condition was attributed as a registration and death to any industry, in this case to the chemical sector. The exposure that was considered relevant was acrylamide.

In summary, there were various historical exposures linked to the chemical sector, which were identified by the Cancer Burden Project, as being relevant for cancer causation. These exposures will retain the ability to cause occupational related cancers. It is currently appropriate to base estimates for the contribution made by the chemical sector to cancer development on those derived in the Cancer Burden Project. It is also important to appreciate that the evidence used to derive these estimates varied in nature, geography, time and population studied, and that estimates were not necessarily based on work within the chemical sector. It is noteworthy that there is currently work underway investigating the future cancer burden due to occupational exposures[55], which takes into account past and projected trends in exposure. The results of the future burden study may provide better estimates for future cancer risks in the chemical sector; however, changing the historical exposures identified in the current Cancer Burden Project may also prevent future cancer.

(v) Occupational Health Decennial Supplement

Reviewing the data for the two time periods studied (1979 to 1990 and 1991 to 2000) enabled useful information relating to disease risk to be compiled for the chemical sector. The identified diseases associated with mortality were generally those expected given the nature of certain

exposures. For example, cancer of the pleura associated with asbestos exposure, and liver cancer seen as elevated presumably as a consequence of vinyl chloride exposure.

Various other diseases were identified to be significantly elevated in chemical workers, either by interpretation of the published data from the two decennial supplements, or by *post hoc* analyses of the supplementary data available from ONS. The latter identified a persistent increased risk of stomach cancer in male chemical workers, although the causative agent is not known. Indeed, this data specifically raises this issue and confirms that a cause for this finding is not identified.

Urothelial cancer and cancer of the kidney in males were also noted to have raised Proportionate Mortality Ratios (PMRs) in the decade 1991 – 2000. Additionally, cancer of the liver had a raised PMR, whilst it is interesting to note that male chemical workers had a low PMR for "other alcohol related disease".

In terms of non-malignant causes of death associated with the chemical sector, poisoning by "other gases" had caused four fatalities in the 1979-1990 time period, but this effect was not seen in the later decade. The PMR for ischaemic heart disease was raised in both time periods. It is not possible to relate this to a specific exposure within the chemical sector, and other explanations for this observed effect might contribute, including an effect of proportional mortality as a consequence of survivorship from other causes of mortality within this occupational group.

In female chemical workers there were no sustained raised PMRs, and the numbers tended to be low within each diagnostic category making these data much more difficult to interpret.

(vi) National Exposure Data Base

National Exposure Data Base derived data was accessed as part of this project. The data identified contributed little to the overall project aim, although the data did identify that, in the case of cobalt and azodicarbonamide, exposures generally exceeded the WELs. Unfortunately no further inference is possible in relation to why this is. Lack of any data relating to clinically relevant issues does raise the issue of limited access to current relevant data either as part of workplace assessment programmes, or as part of research used to assess future ill health risks.

(vii) Industry data

It was not possible to include industry data in this report. However, it was evident that there was a willingness to provide more information where required, but that this provision of internal data would be best as part of a specific project to answer a specific question.

The third main aim of this project was to undertake a scoping review of the peer reviewed published literature. This identified a number of limited review articles and original research articles that were assessed. The scoping review identified papers that contained data that were broadly consistent with the other seven data sources used for this process. In addition, various other diseases and specific exposures were discussed in the relevant papers.

There were various exceptions to the broad consistency between data sources and the literature review. For example, bladder cancer was identified as a risk in chemical exposed workers in the literature review, but not identified for further assessment generally in, for example, the Cancer Burden work. In fact, bladder cancer was identified in the Cancer Burden Project, but was only associated with a small attributable fraction and attributable numbers. Because of this, it was not elaborated on further in the Cancer Burden section.

The findings of this report have implications for stakeholders including: industry bodies for the chemical sector, duty holders and employers, occupational health professionals and other health care professionals. Based on the authors' collective expertise and experience in the control of risks to occupational health, it is suggested that the following three options could be considered by stakeholders for the chemical sector to improve the control of the health risks identified in this study;

(i) Defining educational approaches to improve worker, employer and occupational health knowledge about the health risks associated with chemical exposures, and particularly in relation to long latency conditions such as occupationally related cancers.
(ii) Improving uptake and quality of health surveillance for workers at risk of developing occupational asthma and dermatitis.
(iii) Ensure that systematic workplace investigation of all identified occupational illness cases is carried out to identify root causes and take corrective action to prevent recurrence.
(iv) Continued development of preventative strategies as a key requirement to reducing the future burden of chemical related exposures.

6. REFERENCES

1. ONS. *The Annual Population Survey*. Data request obtained from HSE. 2013
2. Darnton A. *Personal Communication*. HSE Statistics and Epidemiology Unit, 24.5.12
3. HSE. *The burden of occupational cancer in Great Britain. Overview report*. Research Report RR800: Health and Safety Executive. 2010. Available from: http://www.hse.gov.uk/cancer/research.htm
4. COEH. *The Health and Occupation Research network (THOR).* Data request no: 2013-03-HSE, Centre for Occupational and Environmental Health, University of Manchester. 2013
5. HSE. *The burden of occupational cancer in Great Britain. Overview report*. Research Report RR931: Health and Safety Executive. 2012. Available from: http://www.hse.gov.uk/cancer/research.htm
6. Drever F. *Occupational Health Decennial Supplement*. HMSO, London. 1995
7. Coggon D, Harris EC, Brown T, Rice T, Palmer KT. *Occupational mortality in England and Wales, 1991-2000*. Office of Public Sector Information, London. 2009
8. HSE. *The burden of occupational cancer in Great Britain. Methodology*. Research Report RR927: Health and Safety Executive. 2012. Available from: http://www.hse.gov.uk/cancer/research.htm
9. HSE. *The burden of occupational cancer in Great Britain. Technical report: Cancer of the larynx.* Research Report RR855: Health and Safety Executive. 2012. Available from: http://www.hse.gov.uk/cancer/research.htm
10. Shangina O, Brennan P, Szeszenia-Dabrowska N, Mates D, Fabianova E, Fletcher T, T'Mannetje A, Boffetta P, Zaridze D. *Occupational exposure and laryngeal and hypopharyngeal cancer risk in central and eastern Europe*. Am J Epidemiol. 2006;164(4):367-375
11. Soskolne CL, Jhangri GS, Siemiatycki J, Lakhani R, Dewar R., Burch JD, Howe GR, Miller AB. *Occupational exposure to sulfuric acid in southern Ontario, Canada, in association with laryngeal cancer*. Scand J Work Environ Health. 1992;18(4):225-232
12. Steenland K, Schnorr T, Beaumont J, Halperin W, Bloom, T. *Incidence of laryngeal cancer and exposure to acid mists.* Br J Ind Med. 1988;45(11):766-776
13. Brown LM, Mason TJ, Pickle LW, Stewart PA, Buffler PA, Burau K, Ziegler RG, Fraumeni JF Jr. *Occupational risk factors for laryngeal cancer on the Texas Gulf Coast*. Cancer Research. 1988;48(7): 1960-1964
14. Soskolne CL, Zeighami EA, Hanis NM, Kupper LL, Herrmann N, Amsel J, Mausner JS, Stellman JM. *Laryngeal cancer and occupational exposure to sulfuric acid*. Am J Epidemiol. 1984;120(3):358-369
15. HSE. *The burden of occupational cancer in Great Britain. Technical report: Lung cancer*. Research Report RR858: Health and Safety Executive. 2012. Available from: http://www.hse.gov.uk/cancer/research.htm
16. Sorahan T, Burges DC, Hamilton L, Harrington JM. *Lung cancer mortality in nickel/chromium platers, 1946-95*. Occupational and Environmental Epidemiology. 1998;55:236-242
17. Coggon D, Pannett B, Wield G. *Upper aerodigestive cancer in battery manufacturers and steel workers exposed to mineral acid mists*. Occup Environ Med 1996;53:445-449

18. Steenland K, Beaumont J. *Further follow-up and adjustment for smoking in a study of lung cancer and acid mists*. Am J Ind Med. 1989;16:347-354

19. HSE. *The burden of occupational cancer in Great Britain. Technical report: Liver cancer*. Research Report RR857: Health and Safety Executive. 2012. Available from: http://www.hse.gov.uk/cancer/research.htm

20. Boffetta P, Matisane ML, Mundt KA, Dell LD. *Meta-analysis of studies of occupational exposure to vinyl chloride in relation to cancer mortality*. Scand J Work Environ Health. 2003;29:220-229

21. Ward E, Boffetta P, Andersen A, Colin D, Comba P, Deddens JA, DeSantis M, Engholm G, Hagmar L, Langard S, Lundberg I, McElvenney D, Pirastu R, Sali D, Simonato L. *Update of the follow-up of mortality and cancer incidence among European workers employed in the vinyl chloride industry*. Epidemiology 2001;12(2):710-718

22. Kielhorn J, Melber C, Wahnschaffe U. *Vinyl Chloride: still a cause for concern*. Environ Health Perspect. 2000;108(7):579-588

23. Wong O, Whorton MD, Foliart DE, Ragland D. *An industry-wide epidemiologic study of vinyl chloride workers, 1942 - 1982*. Am J Ind Med 1991;20(3):317-334

24. Simonato L, L'Abbe KA, Andersen A, Belli S, Comba P, Engholm G, Ferro G, Hagmar L, Lanqard S, Lundberg I, Pirastu R, Thomas P, Winkelmann R, Saracci R. *A collaborative study of cancer incidence and mortality among vinyl chloride workers*. Scand J Work Environ Health. 1991;17(3):159-169

25. Weber H, Reini W, Greiser E. *German investigations on morbidity and mortality of workers exposed to vinyl chloride*. Environ Health Perspect. 1981;41:95-99

26. Theriault G, Allard P. *Cancer mortality of a group of Canadian workers exposed to vinyl chloride monomer*. Journal of Occupational Medicine 1981;23(10):671-676

27. Wild P, Perdrix A, Romazini S, Moulin JJ, Pellet F. *Lung cancer mortality in a site producing hard metals.* Occup Environ Health. 2000;57:568-573

28. Moulin JJ, Clavel T, Roy D, Dananche B, Marquis N, Fevotte J, Fontana JM. *Risk of lung cancer in workers producing stainless steel and metallic alloys*. Int Arch Occup Environ Health. 2000;73: 171-180

29. Moulin JJ, Wild P, Romazini S, Lasfargues G, Peltier A, Bozec C, Deguerry P, Pellet F, Perdrix A. *Lung cancer risk in hard-metal workers*. Am J Epidemiol. 1998;148:241-248

30. Moulin JJ, Wild P, Mur JM, Fournier-Betz M, Mercier-Gallay M. *A mortality study of cobalt production workers: An extension of the follow-up.* Am J Ind Med. 1993;23:281-288

31. Declos GL, Lerner SP. *Occupational risk factors*. Scand J Urol Nephrol. 2008;42(Supplement 218):58-63

32. Vineis P, Bartsch H, Caporaso N, Harrington AM, Kadlubar FF, Landi MT, Malaveille C, Shields PG, Skipper P, Talaska G, et al. Genetically based N-acetyltransferase metabolic polymorphism and low-level environmental exposure to carcinogens. Nature 1994(12);369(6476):154-6

33. Golka K, Wiese A, Assenato G, Bolt HM. Occupational exposure and urological cancer. World J Urol 2004;21:382-391

34. Brüning T, Bolt HM. Renal toxicity and carcinogenicity of trichloroethylene: key results, mechanisms, and controversies. Crit Rev Toxicol 2000;30(3):253-85.

35. Vamvakas S, Brüning T, Thomasson B, Lammert M, Baumüller A, Bolt HM, Dekant W, Birner G, Henschler D, Ulm K. Renal cell cancer correlated with occupational exposure to trichloroethene. J Cancer Res Clin Oncol 1998;124(7):374-82.

36. Axelson O, Seldén A, Andersson K, Hogstedt C. Updated and expanded Swedish cohort study on trichloroethylene and cancer risk. J Occup Med 1994;36(5):556-62.

37. Heron RJL, Pickering FC. Health effects of exposure to active pharmaceutical ingredients (APIs). Occup Med. 2003;53:357–362

38. Baur X, Latza U. Non-malignant occupational respiratory diseases in Germany in comparison with those of other countries. Int Arch Occup Environ Health. 2005;78:593-602

39. Fairhurst S. Hazard and risk assessment of industrial chemicals in the occupational context in Europe: some current issues. Food Chem Toxicol. 2003;41:1453-1462

40. Morata TC. Chemical exposure as a risk factor for hearing loss. JOEM. 2003;45:676-682

41. Morata TC, Johnson A-C. Effects of exposure to chemicals on noise induced hearing loss. In: LePrell CG et al (eds). Noise induced hearing loss: scientific advances. Springer Handbook of Auditory Research; 2012:40:223-254

42. Julvez J, Grandjean P. Neurodevelopmental toxicity risks due to occupational exposure to industrial chemicals during pregnancy. Industrial Health. 2009;47:459-468

43. Mehlman M. Causal relationship from exposure to chemicals in oil refining and chemical industries and malignant melanoma. Ann N Y Acad Sci. 2006;1076:822-828

44. Hauser R, Calafat AM. Phthalates and human health. Occup Environ Med. 2005;62:806-818

45. Brown SC, Alberts R, Schoenberg M. Cancer incidence and mortality among workers exposed to benzidine. Am J Ind Med. 2011;54(No.4):300-306

46. Van Rooy FGBGJ, Smit LAM, Houba R, Zaat VAC, Rooyackers JM, Heederik DJ. A cross-sectional study of lung function and respiratory symptoms among chemical workers producing diacetyl for food flavourings. Occup Environ Med. 2009;66(No.2):105-110

47. Hanley W, Viet SM, Hein MJ, Carreón T, Ruder AM. Exposure to o-toluidine, aniline, and nitrobenzene in a rubber chemical manufacturing plant: a retrospective exposure assessment update. J Occup Environ Hyg. 2012 Aug; 9(8):478-490

48. Macaluso M, Larson R, Lynch J, Lipton S, Delzell E. Historical estimation of exposure to 1,3-butadiene, styrene, and dimethyldithiocarbamate among synthetic rubber workers. J Occup Environ Hyg. 2004 Jun;1(6):371-390

49. De Vocht F, Sobala W, Wilczynska U, Kromhout H, Szeszenia-Dabrowska N, Peplonska, B. Cancer mortality and occupational exposure to aromatic amines and inhalable aerosols in rubber tire manufacturing in Poland. Cancer Epidemiology 2009;33(No 2): pp269 -273

50. Schubauer Berigan MK, Couch JR, Petersen MR, Carreón T, Jin Y, Deddens JA. Cohort mortality study of workers at seven beryllium processing plants: update and associations with cumulative and maximum exposure. Occup Environ Med. 2011 May;68(5):345-353

51. Thomas CA, Bailey RL, Kent MS, Deubner DC, Kreiss K, Schuler CR. Efficacy of a program to prevent beryllium sensitization among new employees at a copper-beryllium alloy processing facility. Public Health Reports. 2009 Jul-Aug;124(Supplement 1):112-124

52. Park RM, Bena JF, Stayner LT, Smith RJ, Gibb HJ, Lees PSJ. Hexavalent chromium and lung cancer in the chromate industry: a quantitative risk assessment. Risk Anal. 2004 Oct;24(5):1099-1108

53. Brun E. Expert forecast on emerging chemical risks related to occupational safety and health. European agency for safety and health at work. 2009. Found at ; https://osha.europa.eu/en/publications/reports/TE3008390ENC_chemical_risks (last accessed 19.7.2013)

54. Fishwick D, Barber CM, Bradshaw LM, Harris-Roberts J, Francis M, Naylor S, Ayres J, Burge PS, Corne JM, Cullinan P, Frank TL, Hendrick D, Hoyle J, Jaakkola M, Newman-Taylor A, Nicholson P, Niven R, Pickering A, Rawbone R, Stenton C, Warburton CJ, Curran AD; British Thoracic Society Standards of Care Subcommittee Guidelines on Occupational Asthma. Standards of care for occupational asthma. Thorax. 2008 Mar;63(3):240-50. Epub 2007 Sep 28

55. HSE. *Occupational cancer burden research*. Health and Safety Executive. 2012. Available from: http://www.hse.gov.uk/cancer/research.htm

APPENDIX 1

THE CHEMICAL SECTOR STRATEGY DEFINITION

The chemical sector comprises:

- Manufacture of chemicals (including downstream oil and petrochemicals)
- Refining and production of petroleum products
- Import and storage of chemicals and petroleum products
- Chemical storage
- Chemical and petroleum products distribution (excluding pipelines)
- Biological agents - biotech / pharmaceutical production
- Chemical use at work - provision of information / natural use restrictions but risk control only within chemical industries

Further information can be found at:
http://www.hse.gov.uk/aboutus/strategiesandplans/sector-strategies/index.htm

ASSIGNING SIC CODES TO THE CHEMICAL SECTOR STRATEGY DEFINITION

Table A Breakdown of SIC 2003 and SIC 2007 codes included in the definition of the chemicals sector

Chemical Sector Activity	SIC 2003	SIC 2003 Description	SIC 2007	SIC 2007 Description
Manufacture of chemicals (including downstream oil and petrochemicals)	The following components of division 24 "Manufacture of chemicals and chemical products" are relevant:		All components of division 20 "Manufacture of chemicals and chemical products" are relevant:	
	24110	Manufacture of industrial gases	20110	Manufacture of industrial gases
	24120	Manufacture of dyes and pigments	20120	Manufacture of dyes and pigments
	24130	Manufacture of other inorganic basic chemicals	20130	Manufacture of other inorganic basic chemicals
	24140	Manufacture of other organic basic chemicals	20140	Manufacture of other organic basic chemicals
	24150	Manufacture of fertilisers and nitrogen compounds	20150	Manufacture of fertilisers and nitrogen compounds
	24160	Manufacture of plastics in primary forms	20160	Manufacture of plastics in primary forms
	24170	Manufacture of synthetic rubber in primary forms	20170	Manufacture of synthetic rubber in primary forms
	24200	Manufacture of pesticides and other agrochemical products	20200	Manufacture of pesticides and other agrochemical products
	24301	Manufacture of paints, varnishes and similar coatings	20301	Manufacture of paints, varnishes and similar coatings, mastics and sealants
	24302	Manufacture of printing ink	20302	Manufacture of printing ink
	24303	Manufacture of mastics and sealants	20301	Manufacture of paints, varnishes and similar coatings, mastics and sealants
	24511	Manufacture of soap and detergents	20411	Manufacture of soap and detergents
	24512	Manufacture of cleaning and polishing preparations	20412	Manufacture of cleaning and polishing preparations
	24520	Manufacture of perfumes and toilet preparations	20420	Manufacture of perfumes and toilet preparations
	24610	Manufacture of explosives	20510	Manufacture of explosives
	24620	Manufacture of glues and gelatines	20520	Manufacture of glues
	24630	Manufacture of essential oils	20530	Manufacture of essential oils
	24640	Manufacture of photographic chemical material	20590	Manufacture of other chemical products n.e.c.
	24660	Manufacture of other chemical products n.e.c.		
	24700	Manufacture of man-made fibres	20600	Manufacture of man-made fibres

Refining and production of petroleum products	The following components of division 23 "Manufacture of coke, refined petroleum products and nuclear fuel" are relevant:	All components of division 19 "Manufacture of coke and refined petroleum products" are relevant:
	23100 Manufacture of coke oven products 23201 Mineral oil refining 23209 Other treatment of petroleum products (excluding petrochemicals manufacture)	19100 Manufacture of coke oven products 19201 Mineral oil refining 19209 Other treatment of petroleum products (excluding mineral oil refining/petrochemicals manufacture)
Import and storage of chemicals and petroleum products	The following components of division 37 "Recycling", division 51 "Wholesale trade and commission trade, except of motor vehicles and motorcycles" and division 63 "Supporting and auxiliary transport activities; Activities of travel agencies" are relevant:	The following components of division 38 "Waste collection, treatment and disposal activities; materials recovery", division 46 "Wholesale trade, except of motor vehicles and motorcycles" and division 52 "Warehousing and support activities for transportation" are relevant:
	37200 Recycling of non-metal waste and scrap 51120 Agents involved in the sale of fuels, ores, metals and industrial chemicals 51511 Wholesale of petroleum and petroleum products 51519 Wholesale of other fuels and related products 51550 Wholesale of chemical products 63122 Storage of liquids and gases 63129 Other storage and warehousing n.e.c 63110 Cargo handling	38320 Recovery of sorted metals 46120 Agents involved in the sale of fuels, ores, metals and industrial chemicals 46711 Wholesale of petroleum and petroleum products 46719 Wholesale of fuels and related products (other than petroleum and petroleum products) 46750 Wholesale of chemical products 52101 Operation of warehousing and storage facilities for water transport activities of division 50 52102 Operation of warehousing and storage facilities for air transport activities of division 51 52103 Operation of warehousing and storage facilities for land transport activities of division 49 52241 Cargo handling for water transport activities of division 50 52242 Cargo handling for air transport activities of division 51 52243 Cargo handling for land transport activities of division 49

Chemical storage	Some components of division 63 “Supporting and auxiliary transport activities; Activities of travel agencies” are relevant. See above for details	Some components of division 52 “Warehousing and support activities for transportation” are relevant. See above for details
Chemical and petroleum products distribution (excluding pipelines)	The following components of division 60 “Land transport; Transport via pipelines”, division 61 “Water transport” and division 62 “Air transport” are relevant:	The following components of division 49 “Land transport and transport via pipelines”, division 50 “Water transport” and division 51 “Air transport” are relevant:
	60109 Other transport via railways 60249 Freight transport by road n.e.c 61102 Freight sea and coastal water transport 61209 Other inland water transport 62109 Other scheduled air transport 62209 Other non-scheduled air transport	49200 Freight rail transport 49410 Freight transport by road 50200 Sea and coastal freight water transport 50400 Inland freight water transport 51210 Freight air transport
Biological agents - biotech / pharmaceutical production	The following components of division 24 “Manufacture of chemicals and chemical products”, division 51 “Wholesale trade and commission trade, except of motor vehicles and motorcycles” and division 73 “Research and development” are relevant:	All components of division 21 “Manufacture of basic pharmaceutical products and pharmaceutical preparations and the following components of division 46 “Wholesale trade, except of motor vehicles and motorcycles” and division 72 “Scientific research and development” are relevant:
	24410 Manufacture of basic pharmaceutical products 24421 Manufacture of medicaments 24422 Manufacture of non-medicaments 51460 Wholesale of pharmaceutical goods 73100 Research and experimental development on natural sciences and engineering	21100 Manufacture of basic pharmaceutical products 21200 Manufacture of pharmaceutical preparations 32500 Manufacture of medical and dental instruments and supplies 46460 Wholesale of pharmaceutical goods 72110 Research and experimental development on biotechnology 72190 Other research and experimental development on natural sciences and engineering
Chemical use at work	This could cover many SIC codes	This could cover many SIC codes

APPENDIX 2

DISEASES REPORTABLE UNDER RIDDOR 1995

The following conditions are included in the RIDDOR guidance as reportable diseases:

- **Conditions due to physical agents and the physical demands of work**
  - Inflammation, ulceration or malignant disease of the skin due to ionising radiation
  - Malignant disease of the bones due to ionising radiation
  - Blood dyscrasia due to ionising radiation
  - Cataract due to electromagnetic radiation
  - Decompression illness
  - Barotrauma resulting in lung or other organ damage
  - Dysbaric osteonecrosis
  - Cramp of the hand or forearm due to repetitive movements
  - Subcutaneous cellulitis of the hand (beat hand)
  - Bursitis or subcutaneous cellulitis arising at or about the knee due to severe or prolonged external friction or pressure at or about the knee (beat knee)
  - Bursitis or subcutaneous cellulitis arising at or about the elbow due to severe or prolonged external friction or pressure at or about the elbow (beat elbow)
  - Traumatic inflammation of the tendons of the hand or forearm or the associated tendon sheaths
  - Carpal tunnel syndrome
  - Hand-arm vibration syndrome
- **Infections due to biological agents**
  - Anthrax
  - Brucellosis
  - Hepatitis
  - Legionellosis
  - Leptospirosis
  - Lyme disease
  - Q fever
  - Rabies
  - Streptococcus suis
  - Tetanus
  - Tuberculosis
  - Any infection reliably attributable to the performance of the work specified in the following
    - Work with micro-organisms, human beings (providing any treatment, service or investigation involving exposure to blood or body fluids), animals or any potentially infected material derived from any of the above
- **Conditions due to substances**
  - Poisonings
  - Cancer of a bronchus or lung
  - Primary carcinoma of the lung where there is accompanying evidence of silicosis
  - Cancer of the urinary tract
  - Bladder cancer
  - Peripheral neuropathy
  - Chrome ulceration
  - Folliculitis
  - Acne
  - Skin cancer
  - Pneumoconiosis (excluding asbestosis)

    - Byssinosis
    - Mesothelioma
    - Lung cancer
    - Asbestosis
    - Cancer of the nasal cavity or associated air sinuses
    - Occupational dermatitis
    - Extrinsic alveolitis (including farmer's lung)
    - Occupational asthma
- **Additional diseases for offshore work places**
    - Chickenpox
    - Cholera
    - Diphtheria
    - Dysentery
    - Acute encephalitis
    - Erysipelas
    - Food poisoning
    - Legionellosis
    - Malaria
    - Measles
    - Meningitis
    - Meningococcal septicaemia (without meningitis)
    - Mumps
    - Paratyphoid fever
    - Plague
    - Acute poliomyelitis
    - Rabies
    - Rubella
    - Scarlet fever
    - Tetanus
    - Tuberculosis
    - Typhoid fever
    - Thyphus
    - Viral haemorrhagic fevers
    - Viral hepatitis

Further information can be found at:
http://www.hse.gov.uk/riddor/

REPORTED DISEASES WITHIN THE CHEMICAL SECTOR

The detailed records provided further information on the conditions notified under RIDDOR by the chemical sector over the 5-year period of interest.

Table B Breakdown of conditions reported by the chemical sector to RIDDOR over the period 2006/07 to 2010/11

Disease	Total
Conditions due to physical agents and the physical demands of work	
- Bursitis	5 (2%)
- Cramp arm	26 (13%)
- HAVS	6 (3%)
- Inflammation of forearm tendons	28 (14%)
- Other	3 (1%)
Conditions due to substances	
- Occupational asthma	21 (10%)
- Occupational dermatitis	114 (55%)
Other reported conditions	4 (2%)
TOTAL	**207**

APPENDIX 3

ILLNESSES INCLUDED IN THE SWI SURVEY

The following illnesses are included in survey:

- Bone, joint or muscle problems which mainly affect (or is mainly connected with) arms, hands, neck or shoulder
- Bone, joint or muscle problems which mainly affect (or is mainly connected with) hips, legs or feet
- Bone, joint or muscle problems which mainly affect (or is mainly connected with) back
- Breathing or lung problems
- Skin problems
- Hearing problems
- Stress, depression or anxiety
- Headache and/or eyestrain
- Heart disease/attack, other circulatory system
- Infectious disease (virus, bacteria)
- Other

BROAD OCCUPATION CATEGORIES USED AND RELATED SOC CODES (2-DIGIT)

- Office based
    - 11 Corporate managers and directors
    - 12 Other managers and proprietors
    - 24 Business, media and public service professionals
    - 35 Business and public service associate professionals
    - 41 Administrative occupations
    - 42 Secretarial and related occupations
    - 71 Sales occupations
    - 72 Customer service occupations
    - 92 Elementary administration and service occupations
- Laboratory based
    - 21 Science, research, engineering and technology professionals
    - 22 Health professionals
    - 31 Science, engineering and technology associate professionals
    - 32 Health and social care associate professionals
- Factory/warehouse based
    - 33 Protective service occupations
    - 52 Skilled metal, electrical and electronic trades
    - 53 Skilled construction and building trades
    - 81 Process, plant and machine operatives
    - 82 Transport and mobile machine drivers and operatives
    - 91 Elementary trades and related occupations
- Other
    - 23 Teaching and educational professionals
    - 34 Culture, media and sports occupations
    - 51 Skilled agricultural and related trades
    - 54 Textiles, printing and other skilled trades
    - 61 Caring personal service occupations
    - 62 Leisure, travel and related personal service occupations

APPENDIX 4

REPORTED DIAGNOSIS IN THOR BY INDUSTRIAL DIVISION

Table C Breakdown of actual diagnoses reported to THOR within the chemical sector over the period 2006 to 2010, by industrial division

Diagnosis Group/Subgroup	Manufacture of coke, refined petroleum products and nuclear fuel N (%)		Manufacture of chemicals and chemical products N (%)		Total within the Chemical Sector N (%)	
Respiratory	**23**	**(72%)**	**125**	**(39%)**	**148**	**(42%)**
Asthma/allergy	6	(19%)	57	(18%)	63	(18%)
Inhalation accident			8	(3%)	8	(2%)
Cancer (including mesothelioma)	8	(25%)	11	(3%)	19	(5%)
Non-malignant pleural disease	9	(28%)	41	(13%)	50	(14%)
Pneumoconiosis			8	(3%)	8	(2%)
Skin	**9**	**(28%)**	**192**	**(60%)**	**201**	**(57%)**
Dermatitis/urticaria	8	(25%)	173	(54%)	181	(51%)
Other dermatoses	1	(3%)	19	(6%)	20	(6%)
Other			**4**	**(1%)**	**4**	**(1%)**
Total	**32**		**321**		**353***	

* There are 353 diagnosis recorded within the THOR data relating to 352 individual records

REPORTED DIAGNOSIS IN THOR BY BROAD OCCUPATION

Table D Breakdown of diagnoses reported to THOR within the chemical sector over the period 2006 to 2010, by broad occupational category

Occupation	Respiratory		Skin		Other		Total	
Office based	12	(8%)	15	(8%)			**27**	**(8%)**
Laboratory based	25	(17%)	39	(19%)	1	(25%)	**65**	**(18%)**
Factory / warehouse based	105	(71%)	145	(72%)	1	(25%)	**251**	**(71%)**
Other / Unknown	6	(4%)	2	(1%)	2	(50%)	**10**	**(3%)**
Total	**148**		**201**		**4**		**353***	

* There are 353 diagnosis recorded within the THOR data relating to 352 individual records

Further information can be found at:
http://www.medicine.manchester.ac.uk/oeh/research/thor/

APPENDIX 5

Table E Breakdown of the estimated attributable fraction (AF) and attributable registrations (N) within the chemical sector, by CAREX industry, cancer and agent from the Cancer Burden Project

	Petroleum refineries		Manufacture of miscellaneous products of petroleum and coal		Manufacture of industrial chemicals		Manufacture of other chemical products		Total for all CAREX industries combined		
	AF (%)	N	AF (%)	N	AF (%)	N	AF (%)	N	AF (%)	N (95% CI)	
Bladder	**0.00**	**0**	**0.00**	**0**	**0.01**	**1**	**0.00**	**0**	**5.57**	**550**	**(357, 795)**
- Aromatic amines	-	-	-	-	0.00	0	-	-	0.67	66	(30, 147)
- Diesel engine exhaust	0.00	0	-	-	0.00	0	0.00	0	1.08	106	(18, 214)
- PAHs	-	-	0.00	0	0.01	1	-	-	0.07	7	(3, 11)
Brain	**0.01**	**0**			**0.00**	**0**	**0.00**	**0**	**0.35**	**14**	**(1, 28)**
- Inorganic Iead	-	-			0.00	0	0.00	0	0.05	2	0, 13)
- Non-arsenical insecticides	-	-			0.00	0	-	-	0.29	11	(3,20)
- Petroleum refining	0.01	0			-	-	-	-	0.01	0	(0,4)
Larynx	**0.00**	**0**			**0.28**	**6**	**0.34**	**7**	**2.66**	**56**	**(26, 112)**
- Asbestos	0.00	0			0.01	0	0.01	0	0.39	8	(4,13)
- Strong inorganic-acid mists	-	-			0.28	6	0.33	7	2.16	46	(17,102)
Leukaemia	**0.00**	**0**	**0.00**	**0**	**0.01**	**0**	**0.01**	**0**	**0.74**	**38**	**(8, 198)**
- 1,3-Butadiene	0.00	0	-	-	0.00	0	0.00	0	0.01	0	(0, 3)
- Benzene	0.00	0	0.00	0	0.01	0	0.00	0	0.14	7	(0, 128)
- Ethylene oxide	-	-	-	-	-	-	0.01	0	0.01	1	(0, 11)
- Formaldehyde	-	-	-	-	0.00	0	0.00	0	0.20	10	(3, 25)
- Non-arsenical insecticides	-	-	-	-	0.00	0	-	-	0.38	19	(5, 35)
Liver	**0.00**	**0**			**0.04**	**1**	**0.04**	**1**	**0.18**	**5**	**(3, 8)**
- Vinyl chloride	0.00	0			0.04	1	0.04	1	0.11	3	(2,6)
Lung	**0.05**	**20**	**0.00**	**1**	**0.19**	**70**	**0.20**	**75**	**14.22**	**5442**	**(4877, 6469)**
- Arsenic	0.00	0	-	-	0.01	3	0.00	0	0.35	129	(49, 274)
- Asbestos	0.05	20	-	-	0.09	33	0.10	36	5.95	2223	(2032, 2409)
- Cadmium	-	-	-	-	0.00	1	-	-	0.02	9	4, 14)

- Chromium	-	-	-	-	0.01	3	0.00	2	0.18	67	(44, 92)
- Cobalt	0.00	0	-	-	0.02	6	0.03	10	0.19	73	(18, 147)
- Diesel engine exhaust	0.00	0	0.00	0	0.00	1	0.00	1	1.86	695	(313, 1269)
- Inorganic Iead	-	-	-	-	0.00	1	0.01	2	0.11	41	(0, 149)
- PAHs	0.00	0	0.00	0	0.00	0	-	-	0.00	1	(0, 1)
- Radon	0.00	0	0.00	0	0.00	2	0.01	2	0.56	209	(105, 314)
- Silica	-	-	0.00	1	0.00	1	0.03	10	2.43	907	(680, 1147)
- Strong inorganic-acid mists	-	-	-	-	0.03	11	0.03	13	0.20	76	(0, 207)
- TCDD	-	-	-	-	0.02	8	-	-	0.57	215	(0, 559)
Lymphohaematopoietic	**0.00**	**0**			**0.00**	**0**	**0.00**	**0**	**0.00**	**1**	**(0, 2)**
- 1,3-Butadiene	0.00	0			0.00	0	0.00	0	0.00	1	(0, 2)
Mesothelioma*	**0.86**	**18**			**1.48**	**30**	**1.58**	**32**	**78.65**	**1602**	
- Asbestos	0.86	18			1.48	30	1.58	32	78.65	1602	
Multiple Myeloma					**0.00**	**0**			**0.33**	**10**	**(0, 21)**
- Non-arsenical insecticides					0.00	0			0.33	10	(0, 21)
NHL					**0.05**	**4**			**1.70**	**140**	**(3, 430)**
- Non-arsenical insecticides					0.02	1			0.40	33	(16, 50)
- TCDD					0.03	3			0.90	74	(0 346)
Oesophagus	**0.00**	**0**							**2.51**	**188**	**(80, 439)**
- Tetrachloroethylene	0.00	0							1.73	130	(31, 377)
Pancreas					**0.01**	**1**	**0.00**	**0**	**0.01**	**1**	**(0, 4)**
- Acrylamide					0.01	1	0.00	0	0.01	1	(0, 4)
Sinonasal	**0.03**	**0**			**0.19**	**1**	**0.11**	**0**	**33.41**	**126**	**(83, 212)**
- Chromium	0.03	0			0.18	1	0.10	0	5.79	22	(8, 59)
- Wood dust	0.00	0			0.01	0	0.02	0	10.35	39	(15, 76)
Skin (NMSC)	**0.01**	**7**							**4.26**	**2862**	**(478, 6346)**
- Solar radiation	0.01	7							2.29	1541	(735, 2419)
Soft tissue sarcoma					**0.05**	**1**			**2.50**	**27**	**(0, 90)**
- TCDD					0.05	1			2.50	27	(0, 90)
Stomach	**0.01**	**0**			**0.02**	**2**	**0.02**	**2**	**1.98**	**157**	**(81, 274)**
- Asbestos	0.01	0			0.01	1	0.01	1	0.59	47	(36, 60)
- Inorganic lead	-	-			0.01	1	0.01	1	0.28	23	(13, 35)
TOTAL		**46**		**1**		**116**		**119**		**13598**	**(9303, 20206)**
RANK		**33**		**58**		**19**		**18**			

Table F Breakdown of the estimated attributable fraction (AF) and attributable deaths (N) within the chemical sector, by CAREX industry, cancer and agent from the Cancer Burden Project

	Petroleum refineries		Manufacture of miscellaneous products of petroleum and coal		Manufacture of industrial chemicals		Manufacture of other chemical products		Total for all CAREX industries combined		
	AF (%)	N	AF (%)	N	AF (%)	N	AF (%)	N	AF (%)	N (95% CI)	
Bladder	**0.00**	**0**	**0.00**	**0**	**0.01**	**0**	**0.00**	**0**	**5.57**	**245**	**(159, 358)**
- Aromatic amines	-	-	-	-	0.00	0	-	-	0.67	31	(14, 69)
- Diesel engine exhaust	0.00	0	-	-	0.00	0	0.00	0	1.08	47	(8, 94)
- PAHs	-	-	0.00	0	0.01	0	-	-	0.07	3	(1, 5)
Brain	**0.01**	**0**			**0.00**	**0**	**0.00**	**0**	**0.35**	**11**	**(1, 23)**
- Inorganic Iead	-	-			0.00	0	0.00	0	0.05	2	(0, 11)
- Non-arsenical insecticides	-	-			0.00	0	-	-	0.29	9	(2, 17)
- Petroleum refining	0.01	0			-	-	-	-	0.01	0	(0, 3)
Larynx	**0.00**	**0**			**0.28**	**2**	**0.34**	**3**	**2.66**	**20**	**(9, 40)**
- Asbestos	0.00	0			0.01	0	0.01	0	0.39	3	(1, 5)
- Strong inorganic-acid mists	-	-			0.28	2	0.33	3	2.16	16	(6, 36)
Leukaemia	**0.00**	**0**	**0.00**	**0**	**0.01**	**0**	**0.01**	**0**	**0.74**	**23**	**(5, 120)**
- 1,3-Butadiene	0.00	0	-	-	0.00	0	0.00	0	0.01	0	(0, 2)
- Benzene	0.00	0	0.00	0	0.01	0	0.00	0	0.14	4	(0, 78)
- Ethylene oxide	-	-	-	-	-	-	0.01	0	0.01	0	(0, 7)
- Formaldehyde	-	-	-	-	0.00	0	0.00	0	0.20	6	(2, 15)
- Non-arsenical insecticides	-	-	-	-	0.00	0	-	-	0.38	12	(3, 21)
Liver	**0.00**	**0**			**0.04**	**1**	**0.04**	**1**	**0.18**	**5**	**(3, 8)**
- Vinyl chloride	0.00	0			0.04	1	0.04	1	0.11	3	(2, 6)
Lung	**0.05**	**18**	**0.00**	**0**	**0.19**	**61**	**0.20**	**66**	**14.22**	**4745**	**(4251, 5643)**
- Arsenic	0.00	0	-	-	0.01	3	0.00	0	0.35	113	(43, 240)
- Asbestos	0.05	17	-	-	0.09	29	0.10	31	5.95	1937	(1770, 2100)
- Cadmium	-	-	-	-	0.00	1	-	-	0.02	8	(4, 12)
- Chromium	-	-	-	-	0.01	3	0.00	1	0.18	58	(38, 81)
- Cobalt	0.00	0	-	-	0.02	5	0.03	9	0.19	63	(16, 128)
- Diesel engine exhaust	0.00	0	0.00	0	0.00	1	0.00	1	1.86	605	(272, 1107)

- Inorganic Iead	-	-	-	-	0.00	1	0.01	2	0.11	36	(0, 130)
- PAHs	0.00	0	0.00	0	0.00	0	-	-	0.00	1	(0, 1)
- Radon	0.00	0	0.00	0	0.00	1	0.01	2	0.56	184	(92, 276)
- Silica	-	-	0.00	0	0.00	1	0.03	9	2.43	789	(592, 998)
- Strong inorganic-acid mists	-	-	-	-	0.03	9	0.03	11	0.20	67	(0, 181)
- TCDD	-	-	-	-	0.02	7	-	-	0.57	187	(0, 488)
Lymphohaematopoietic	**0.00**	**0**			**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**(0, 1)**
- 1,3-Butadiene	0.00	0			0.00	0	0.00	0	0.00	0	(0, 1)
Mesothelioma*	**0.86**	**18**			**1.48**	**30**	**1.58**	**32**	**78.65**	**1602**	
- Asbestos	0.86	18			1.48	30	1.58	32	78.65	1602	
Multiple Myeloma					**0.00**	**0**			**0.33**	**6**	**(0, 12)**
- Non-arsenical insecticides					0.00	0			0.33	6	(0, 12)
NHL					**0.05**	**2**			**1.70**	**57**	**(1, 176)**
- Non-arsenical insecticides					0.02	1			0.40	13	(7, 21)
- TCDD					0.03	1			0.90	31	(0, 142)
Oesophagus	**0.00**	**0**							**2.51**	**184**	**(78, 429)**
- Tetrachloroethylene	0.00	0							1.73	126	(30, 368)
Pancreas					**0.01**	**1**	**0.00**	**0**	**0.01**	**1**	**(0, 4)**
- Acrylamide					0.01	1	0.00	0	0.01	1	(0,4)
Sinonasal	**0.03**	**0**			**0.19**	**0**	**0.11**	**0**	**33.41**	**38**	**(25, 63)**
- Chromium	0.03	0			0.18	0	0.10	0	5.79	7	(3, 18)
- Wood dust	0.00	0			0.01	0	0.02	0	10.35	12	(4, 23)
Skin (NMSC)	**0.01**	**0**							**4.26**	**23**	**(0, 52)**
- Solar radiation	0.01	0							2.29	12	(6, 19)
Soft tissue sarcoma					**0.05**	**0**			**2.50**	**13**	**(0, 45)**
- TCDD					0.05	0			2.50	13	(0, 45)
Stomach	**0.01**	**0**			**0.02**	**1**	**0.02**	**1**	**1.98**	**108**	**(55, 187)**
- Asbestos	0.01	0			0.01	1	0.01	1	0.59	32	(24, 41)
- Inorganic lead	-	-			0.01	0	0.01	1	0.28	16	(9, 24)
TOTAL		**36**		**1**		**99**		**103**		**8010**	**(6888, 9977)**
RANK		**28**		**58**		**14**		**13**			

Table G Laryngeal and Lung cancer: Studies considered for exposure to strong inorganic acid mists containing sulphuric acid [* (Red text) indicates the estimates chosen by the Cancer Burden study team]

Reference	Country	Study Population	Study Period	Study size	Comments	Larynx Results	Lung Results
Shangina *et al* (2006)	Romania, Poland, Russia, Slovakia	Hospital	1999-2002	316 M cases 728 M controls	Adjusted for tobacco and alcohol	OR=0.94 (0.60-1.49)	
Soskolne *et al* (1992)	Canada	Population	1977-1979	204 cases 204 controls	Adjusted for tobacco and alcohol	Total: OR=2.90 (1.62-5.20) * Low: OR=1.91 (0.97-3.78) * High: OR=4.28 (2.13-8.58)	
Steenland *et al* (1988)	US	Metal treatment industry	Employed 1940-1965	1,156 M	Adjusted for tobacco and alcohol	SIR=2.2 (1.2-3.7)	
Brown *et al* (1988)	US	Hospital	1980-1981	183 M cases 250 M controls	Adjusted for tobacco and alcohol	RR=0.76 (0.42-1.35)	
Soskolne *et al* (1984)	US	Chemical workers	1944-1980	80 M cases 175 M controls	Adjusted for tobacco and alcohol	Moderate: OR=4.6 (0.83-25.4) High: OR=13.4 (2.08-86.0)	
Sorahan *et al* (1998)	UK	Chrome bath workers	Employed 1946-1975 Follow-up 1946-1995	812 M 49 deaths 950 F 16 deaths			Males: SMR=1.25 (0.93-1.66) Females: SMR=1.24 (0.71-2.01)
Coggon *et al* (1996)	Britain	Battery plants and steel works	Follow-up to 1993	4,401 134 deaths	* An RR of 1.0 is used for the low exposure group		Never: SMR=0.94 (0.78-1.11) Possible: SMR=0.77 (0.54-1.07) * Definite: SMR=0.98 (0.78-1.22)
Steenland & Beaumont (1989)	US	Steel workers	Employed <1965 Follow-up to 1986	1,165 41 deaths	Adjusted for smoking		* SMR=1.36 (0.97-1.84)

Table H Liver cancer: Studies considered for exposure to vinyl chloride [* (Red text) indicates the estimates chosen by the cancer burden study team]

Reference	Country	Study Population	Study Period	Study size	Comments	Liver Results
Boffetta *et al* (2003)					Meta-analysis	SMR=2.52 (1.56-4.07)
Ward *et al* (2001)	Europe			12,700		SMR=2.4 (1.8-3.1)
Kielhorn *et al* (2000)	See below			81 deaths		SMR=5.33 (4.23-6.62)
Wong *et al* (1991)	US	Plants	Employed <1973 Follow-up 1942-1982	10,173 M 37 deaths		SMR=6.41 (4.5-8.84)
Simonato *et al* (1991)	Europe	Factories	Follow-up 1955-1986	14,351 24 deaths		* SMR=2.86 (1.83-4.25)
Weber *et al* (1981)	Germany	VC exposed workers		12 deaths		SMR=15.23
Theriault & Allard (1981)	Canada	VC exposed workers		8 deaths		SMR=57.14
					Harmonic mean used for low exposure * RR=1.89 (0.32-3.96)	

Table I Lung cancer: Studies considered for exposure to cobalt [* (Red text) indicates the estimates chosen by the Cancer Burden study team]

Reference	Country	Study Population	Study Period	Study size	Comments	Lung Results
Wild et al (2000)	France	Production site		2,860 46 deaths		SMR=1.70 (1.24-2.26)
Moulin et al (2000)	France	Steel workers		4,897 54 deaths Nested study: 17 exposed cases 67 exposed controls	Nested study adjusted for smoking	SMR=1.20 (0.90-1.57) Nested study: OR=0.57 (0.16-1.14)
Moulin et al (1998)	France	Hard metals industry	Follow-up 1968-1991	7,459 63 deaths Nested study: 61 cases 180 controls		* SMR=1.30 (1.00-1.66) Nested study: * OR=1.93 (1.03-3.62)
Moulin et al (1993)	France	Electro-chemical plant: cobalt production	Employed 1950-1980 Follow-up to 1988	1,148 M 8 deaths		Only production: SMR=1.16 (0.24-3.46) Ever production: SMR=1.8 (0.32-3.03)

APPENDIX 6

OCCUPATIONAL HEALTH DECENNIAL SUPPLEMENT

Chemical engineers and scientists

Table J Causes of death and cancer registrations with statistically significant PMRs and PRRs for chemical engineers and scientists. Men aged 20-74 years, England, 1979-90 [Black text indicates excess. *(Red text) indicates deficit]

Cause of death / Diagnosed cancer	Deaths (1979 – 1980 and 1982 – 1990)	PMR	95% CI	Registrations (1981 – 1987)	PRR	95% CI
Men						
Cancer of the pleura	13	238	127-406			
Chronic rheumatic heart disease	20	198	121-306			
* Hypertensive disease	10	50	24-92			
Injury undetermined whether accidentally or purposely inflicted	29	183	122-263			
Chronic lymphatic leukaemia				7	270	109-557

Table K Causes of death with statistically significant PMRs for chemical engineers and scientists. Men and women aged 16-74 years, England, 1991-2000 [Black text indicates excess. *(Red text) indicates deficit]

Cause of death	Deaths (1991-2000)	PMR	95% CI
Men			
* HIV	0	0	0-89
Cancer of the pleura	14	190	104-319
Meningeal tumour	6	351	129-764
* Non-Hodgkin's lymphoma	30	69	47-99
* Parkinson's disease	4	36	10-91
Multiple sclerosis	13	194	103-332
Women			
Cancer of the rectum	6	463	170-1008
Peripheral valve disease	3	863	178-2523

Chemical workers

Table L Causes of death and cancer registrations with statistically significant PMRs and PRRs for chemical workers. Men and women aged 20-74 years, England, 1979-90 [Black text indicates excess. *(Red text) indicates deficit]

Cause of death / Diagnosed cancer	Deaths (1979 – 1980 and 1982 – 1990)	PMR	95% CI	Registrations (1981 – 1987)	PRR	95% CI
Men						
Cancer of the stomach	448	111	101-122			
Cancer of the pleura	39	159	113-217			
* Epilepsy	18	59	35-93			
Ischaemic heat disease	5477	104	101-107			
* Pulmonary embolism and phlebitis	81	77	61-96			
* Chronic and unspecified myocarditis	8	30	13-60			
Sub-arachnoid haemorrhage	104	122	100-148			
* Bronchopneumonia	257	83	73-94			
* Chronic bronchitis and emphysema	815	87	81-93			
* Asthma	35	67	47-94			
* Coal workers' pneumoconiosis	2	9	1-32			
* Cirrhosis of the liver	30	68	46-98			
Poisoning by other gases	4	1093	298-2798			
* Injury by falling object	2	23	3-85			
Injury by machinery	22	199	125-302			
Injury by explosive material	12	797	412-1392			
Injury by hot substances	5	559	182-1305			
* Injury undetermined whether accidentally or purposely inflicted	55	64	48-83			
Pleura				30	169	114-242
Women						
Cancer of the pleura	4	498	136-1275			
* Urothelial cancer	0	0	0-46			
* Aortic aneurysm	3	32	7-93			
Stomach				31	185	126-263
All Leukaemia				18	305	181-483
- Acute myeloid leukaemia				10	382	183-703
- Other leukaemia				3	558	115-1632
* Female breast				69	73	58-94

Table M Causes of death with statistically significant PMRs for chemical workers. Men and women aged 16-74 years, England, 1991-2000 [Black text indicates excess. *(Red text) indicates deficit]

Cause of death	Deaths (1991-2000)	PMR (1991-2000)	95% CI (1991-2000)
Men			
Cancer of the stomach	218	121	105-138
Cancer of the liver	56	137	103-177
Urothelial cancer	123	124	103-148
Cancer of the kidney (except pelvis)	90	144	115-177
Dementia	42	143	103-194
* Other alcohol-related diseases	63	74	57-95
Ischaemic heart disease	2682	106	102-110
* Other cerebrovascular disease	436	90	81-98
* Asthma	12	51	26-89
* Coal worker's pneumoconiosis	1	8	0-42
Silicosis	4	491	134-1257
Fibrosing alveolitis	38	153	109-211
Glomerulonephritis	10	262	126-482
* Infections of skin, joints and bones	0	0	0-75
* Motor vehicle traffic accidents	25	48	31-71
* Accidental poisoning by drugs	2	17	2-61
* Injured by fire	1	16	0-91
* Suicide	48	50	37-67
* Injury undetermined as accidental or purposely inflicted	20	48	30-75
Women			
Hypertensive disease	11	221	111-396
Ischaemic heart disease	192	116	100-134
* Motor vehicle traffic accidents	0	0	0-94
* Injury undetermined as accidental or purposely inflicted	0	0	0-88

APPENDIX 7

CHEMICAL SECTOR DEFINITION USED FOR NEDB SEARCH

The following terms were searched in the NEDB:

- Basic Industrial Chemicals Manufacture (SIC 24.1)
- Manufacture of Other Chemical Products not elsewhere classified (SIC 24.66)
- Manufacture of Other Inorganic Basic Chemicals (SIC 24.13)
- Manufacture of Other Organic Basic Chemicals (SIC 24.14)
- Manufacture of Refined Petroleum Products (SIC 23.20)
- Other treatment of petroleum products (excluding petrochemicals) (SIC 23.20/9)
- Specialised Chemical Products Manfr (SIC 24.6)
- Wholesale of chemical products (SIC 51.55)
- Manufacture of Refined Petroleum Products (SIC 23.20)
- Other treatment of petroleum products (excluding petrochemicals) (SIC 23.20/9)
- Wholesale of petroleum and petroleum products (SIC 51.51/1)
- Manufacture of Basic Pharmaceutical Products (SIC 24.41)
- Manufacture of Pharmaceutical preparations (SIC 24.42)
- Wholesale of pharmaceutical goods (SIC 51.46)

APPENDIX 8

LITERATURE REVIEW SEARCH CRITERIA

The following search criteria were used to search for relevant literature:

Date range 2002 to 2012
Specific Disease terms:

- Carcinogens
- Dermatitis
- Asthma
- Chronic Obstructive Pulmonary Disease
- Endocrine

Industry terms:

- Manufacture of chemicals
- Import of chemicals
- Chemical storage
- Chemical distribution
- Biotechnology & pharmaceutical production
- Nanotechnology

Search strategies:

- AND hazard* or expos* or overexpos* or harm* or injur* or ailment* or health* or ill* or disease* or hygiene or impair* or factor* or effect* or program* or control* or evaluat* or prevent* or protect* or impact* or surveillance or risk*
  (This includes the most sensitive search strategy for OSH studies in Pubmed, including non-randomised intervention studies from the Cochrane library)
- AND chemical* or substance* or dust* or vapour* or fume* or gas*or fibre* or mist* or metal* or paint* or flux* or resin* or adhesive* or solvents*

Other Inclusion/Exclusion Criteria:

- Published (peer reviewed) literature only
- From present day to last 10 years
- Global search (not restricted to UK only papers)
- English language only
- Case reports and narratives included

Databases:
Oshrom, Web of Science, OshUpdate, Healsafe, Embase, Medline, Chemical Engineering abstracts, Chemical Safety Newsbase, Toxfile

Published by the Health and Safety Executive 08/14

HSE

Health and Safety Executive

Research to determine the incidence, prevalence and relative risk of ill health due to chemical exposure in the chemical and downstream oil industry sector

This project identified seven data sources from which to assess ill health problems potentially associated with exposure to harmful chemicals in the chemical and downstream oil industry. Interrogation of these sources allowed insight into the range and type of ill health previously, and currently, associated with certain exposures. A bespoke definition of the chemical and downstream oil industry sector, based on SIC codes, was developed as part of this project in order to assist this process.

It was written to:

- define the scope of the term 'Chemical Sector'.
- review and critically appraise the data sources of reported ill health and related exposure data in order to better understand these relationships in the chemical sector.
- undertake a scoping review of the peer reviewed published literature to establish the range and type of reported industry sector causes of occupational ill health due to chemicals.
- use this information to identify which particular industries within the chemical sector may have previously described high levels of work-related ill health.

This report and the work it describes were funded by the Health and Safety Executive (HSE). Its contents, including any opinions and/or conclusions expressed, are those of the authors alone and do not necessarily reflect HSE policy.

RR1013

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