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Research into Malignant and Non-malignant Respiratory Disease Prescriptions: Phase 3 Summary Report

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Contents

1 Introduction 4
2 Methods 5
3 Results 7
3.1 Silica and COPD 7
3.2 Silica and Lung Cancer 8
3.3 Cleaning and COPD 8
3.4 Farming and COPD 9
3.5 Chromium VI and Lung Cancer 10
3.6 Asbestos and Lung Cancer 10
4 Conclusions 12
Appendix- Relevant current prescriptions 14

1 Introduction

This project had the overall aim of undertaking a review of the occupational causes of respiratory cancers and chronic obstructive pulmonary disease (COPD) with a view to producing evidence for the Industrial Injuries Advisory Council (IIAC) to consider in recommending any changes to current prescriptions for these diseases.

The project was split into three phases:

1. To do a search of reviews (preferably systematic reviews and/or meta-analyses, but narrative reviews or large studies if neither of these were available) carried out in the past 10 years or so and to discuss and agree priorities with IIAC for which exposure/disease outcome combinations should be looked at in more detail. It was agreed that the focus should be on respiratory cancers and/or chronic obstructive pulmonary disease (COPD) only. Occupational asthma was specifically excluded from consideration.
2. Having agreed with IIAC the six most important exposure-disease combinations, to carry out a high-level review to determine which association(s) were worthy of further consideration for prescription by IIAC, and to recommended possibly fruitful further work that IIAC might consider.
3. To summarise the findings in a succinct final report.

2 Methods

In Phase 1, the intention was to identify potential associations of relevance from several sources including a literature search. For the literature search, searches were developed, piloted and run for systematic reviews and/or meta-analyses for occupational causes of respiratory cancer and COPD. This was to identify those occupations and agents (or work circumstances) that might give rise to robust evidence of a doubling of the relative risk on further inspection. The searches also enabled some associations, which might have been of *a priori* interest, where there was a lack of epidemiological evidence, to be set aside and not investigated further.

It was intended that additional sources be used to determine which associations should be candidates for further consideration. These were:

- Associations previously considered by IIAC (and which resulted in command papers/prescriptions, position papers or information notes);
- Occupational associations where the International Agency for Research on Cancer (IARC) consider the human epidemiological evidence of carcinogenicity to be sufficient (cancer only);
- Associations considered by the Health and Safety Executive's (HSE) Workplace Health Expert Committee (WHEC) in the form of a published report;
- Associations listed as known and suspected risk factors on UK respiratory cancer and respiratory disease charities' websites;
- Associations considered as potential priorities by HSE's occupational respiratory physicians; and
- Associations considered as *a priori* potential priorities by IIAC.

The references identified from the database searches were screened and categorised using responses to the following questions for each paper:

a. Is this a review paper [Systematic review; Other Review; No]
b. Does it deal with a relevant health outcome [Yes; No]
c. Is this a study of occupation(s) or substances(s) [Yes; No]
d. Is this a study of occupational exposure [Yes, No]
e. Is this a study of specific substances? [Yes, No]

If the response to any of questions a-c was 'No' then the paper was excluded from further consideration. For included papers, details on the specific health outcome, occupation and/or substance addressed in the paper were recorded.

Prioritisation criteria were developed in consultation with IIAC. These were applied and some tentative exposure-response combinations were presented to IIAC for consideration. These priorities were refined in consultation with IIAC and a final set of six exposure-disease combinations for more detailed investigation were agreed.

For each of the six priority exposure-disease combinations, a literature search was carried out, and the bibliographies of the previously-identified reviews were screened for relevant studies. These were summarised (making use of the most recent IARC reviews for those involving cancer) and the findings analysed for relevance (which was in relation to any existing prescriptions, where appropriate).

Finally, recommendations were tentatively made for future work by IIAC.

3 Results

Initial Criteria were proposed as follows:
Initial Criteria:

- Identified from all of the sources set out the Methods section above:
  - Literature Search of systematic reviews and meta-analyses;
  - IARC agents with sufficient human epidemiological evidence;
  - IIAC command papers, position papers and information notes;
  - Report by HSE WHEC committee;
  - Listed by relevant UK Charities as known/suspected causes on their websites;
  - *A priori* considered potentially important by HSE respiratory physicians; and
  - *A priori* considered potentially important by IIAC.

Main prioritisation Criteria (used to rank those associations meeting the initial criteria):

- Estimated annual number of cases in the UK (as determined by attributable fraction studies and some evidence of a likely raised RR (and therefore a prospective of identifying a sub-population with RR > 2); (i.e. captures associations with large number of cases, but also rarer associations where RR quite high)
- Reviewed by IIAC in the past, but significant recent epidemiology since the last review of the epidemiology;
- Not previously considered by IIAC, but significant recent epidemiology; and
- Relevant for the UK.

Additional criteria:

- Sufficient volume of epidemiological literature;
- Reasonable possibility of being able to define at least one administratively workable exposure situation;
- Sufficient information on exposure-response;
- Evidence provides ability to deal with the confounding effects of tobacco smoking; and
- Can document where the key exposures have taken place.

Application of these criteria in collaboration with IIAC resulted in the following six priority exposure-disease combinations being agreed upon for more detailed investigation:

- Silica and COPD;
- Silica and Lung Cancer (especially in the absence of silicosis);
- Cleaning work and COPD;
- Farming and COPD;
- Chromium VI compounds and Lung cancer; and
- Asbestos and Lung cancer (especially in the absence of asbestosis).

3.1 Silica and COPD

Our search of the epidemiological literature for relevant epidemiological evidence for silica and COPD yielded eight cohort and four case-control studies.

The evidence for a causal association between silica and COPD seemed relatively strong, especially as there seemed quite robust evidence for the existence of an exposure-response relationship. However, the studies remained quite heterogeneous in terms of occupations and industries covered, as did the approaches taken for exposure assessment.

There was evidence of a doubled relative risk for manufacturing plants with high silica exposure (foundries, aircraft manufacturing, oil extraction). However, it was not clear if the risk was spread across all these facilities or concentrated in some of them. There was some evidence of a doubling of the RR in another cohort study of foundry workers, suggesting that these may be the workers in the previous study who were most at risk of COPD. There was an indication of an increased RR at a nuclear weapons facility which suggested there may be a silica exposure level at which the RR was doubled. (This would need further investigation.) A case-control study in construction showed evidence of a doubled RR of COPD.

3.2 Silica and Lung Cancer

What is clear from the epidemiological literature is that there was sufficient epidemiological evidence that occupational exposure to respirable crystalline silica increases the risk of lung cancer and there exists an exposure-response relationship for the association. This was regardless of whether those so exposed develop silicosis or not.

The question now becomes: for which of the industries in which silica is at a sufficient level of exposure are there occupational circumstances in which the RR is doubled?

For diatomaceous earth workers, there was some early evidence from the studies published in the last century that the RR was doubled. However more recent studies show a lack of evidence of a doubled RR. Further work could usefully be undertaken to consider the exposure levels to silica in this industry and how they compare to the levels in other industries in this report.

For metallic ore mining there was evidence of an association between silica and lung cancer, but insufficient evidence that the RR was doubled, especially in studies where there were good controls for smoking and occupational confounders such as asbestos, diesel engine exhaust and radon. As for the diatomaceous earth workers, it would be useful to consider silica exposure levels in this industry in the UK context.

For the single study of coal mining included in this review, there was no evidence of increased lung cancer. However, it would be worth looking at the analysis of the Lady Victoria mine (which had exposure to high levels of silica from cutting through a sandstone seam to see whether coal miners with high silica exposure should be considered for prescription.

There was some evidence that prolonged exposure to silica in the quarry industry may confer a doubled relative risk. This literature would benefit from a closer examination to determine if this degree of exposure could be identified and whether it could be converted to something that DWP decision makers could work with. The same is true for sand and gravel workers.

There is inconsistent evidence of a doubled RR of lung cancer in foundry workers. The literature as a whole would need further examination, both in terms of silica exposure, but also in terms of other co-exposures to lung carcinogens e.g. arsenic, chromium VI and nickel, as well as PAHs.

There is a lack of doubled RRs from the other industries and from the population-based studies.

It would also be worth IIAC examining relative silica exposures in any other industries so see if those occupations with particularly high exposures to silica (e.g. stonemasons) have a doubled RR in epidemiological studies.

3.3 Cleaning and COPD

Our search of the literature for relevant epidemiological evidence for cleaning products and COPD yielded four cohort studies and one case-control design. Two of the cohort studies examined risks in cleaners and the other two assessed risks in nurses. An important methodological limitation to the studies of cleaners was the comparison to the reference categories of managerial or non-manual occupations. While some risk excesses were observed in these studies, due to the limited exposure information, it is not possible to attribute these increases to cleaning products rather than other

differences between occupational groups (e.g., socioeconomic position). Unadjusted SMRs for COPD were increased above 2.00 in one study, but were below 2.00 after adjustment for education, and may have been further attenuated with the addition of smoking adjustment. Another possible limitation of these studies is the challenge to differentiate COPD from asthma.

One of the nurses studies used a job task exposure matrix (JTEM) to characterise frequency of use of cleaning products. A review of nurses' working time suggests <10% of their time is spent on cleaning activities. Importantly, trends of higher risks for more frequent use were significant. This internal comparison helps strengthen the interpretation of risks that are more difficult to assess between occupations. The other nurse study suggested a doubling of risk for the development of COPD in those with the most operating room experience. However, with combined exposure to disinfectants and surgical smoke, it was difficult to separate the risk solely for cleaning product exposure.

The sole case-control study nested within a large population-based cohort of women presented evidence of risks of asthma/bronchitis symptoms in excess of a doubling for intermediate and high exposure to bleach. By contrast, there were significant inverse risks for the use of multi-use cleaners. Ultimately, there were only 3 COPD cases in this study, so, in combination with a relatively small sample size (n= 40 cases), inferences from these results were limited.

3.4 Farming and COPD

Our search of the literature for relevant epidemiological evidence for agricultural exposures and COPD yielded five cohort studies and three relevant case-control studies. The searches were focused on studies specifically of agriculture and farming, and not on exposure to organic dusts more widely. As such, we cannot in this review comment on the associations COPD and organic dust exposure in general.

Three of the cohort studies were population-based studies and two were studies of groups of farmers; all of the studies adjusted for smoking in their analyses. Two of the population studies were based on low numbers of farmers (30 farmers total, and 20 farmers exposed to pesticides respectively), and both studies used non-standard definitions of COPD. One study reported findings for 'chronic non-specific lung disease' which, based on the symptoms analysed, could encompass chronic bronchitis, asthma, COPD or a combination of these, while another study used self-reports of COPD rather than medical diagnosis. After adjustment for smoking, a significantly raised OR for self-reported COPD was seen among the 20 farmers exposed to pesticides, but due to the small number of subjects, and the self-reported health outcomes, inferences from this study were limited. The third population study included over 1,000 farmers and diagnosed airflow obstruction from spirometric readings of FEV_1 and FEV_1/FVC ratio. This study showed a significant association between airflow obstruction and working in hog and/or chicken confinement with an OR of 2.2.

In the two studies of farmers, one study compared agricultural exposures among farmers with COPD to those without COPD. The study used self-reported rather than medically diagnosed occurrence of COPD. The study showed higher levels of exposure to raising hogs among farmers with COPD and chronic bronchitis, but the study did not provide ORs for farmers in relation to other occupational groups. Another study compared risk of chronic bronchitis among dairy and non-dairy farmers with risks in administrative workers. The study was based on small numbers of cases (8 among dairy farmers, 3 among non-dairy farmers and 1 in the controls) resulting in wide 95% CIs and non-significantly raised ORs.

Similarly, two of the three case-control studies investigated the impact of different agricultural practices on occurrence of lung disease within groups of farmers, rather than comparing farmers to other occupational groups or to the general population. The first investigated exposure to plant mould among farmers with and without chronic bronchitis and found no differences between the two groups. The other compared occurrence of COPD in farmers using traditional and modern housing systems on their farms and found significantly increased prevalence of COPD among those using traditional methods, particularly among smokers. The third case-control study compared risk of COPD in farmers compared to office workers. The authors reported significantly increased ORs of 8.13 (univariable analysis) and 15.1 (after adjustment for smoking and other factors), and evidence of an increasing risk with increasing years of exposure. These findings were based on 13 cases of COPD among 21 farmers in the study.

3.5 Chromium VI and Lung Cancer

For lung cancer following exposure to hexavalent chromium, the most recent IARC Monograph stated that almost all of the relative risk estimates were greater than 1.0. Among chromate production workers, virtually all studies showed excess risks of lung cancer, except for a few estimates of risks for US workers hired since exposures were lowered, but these latter analyses had few subjects and low statistical power.

Similarly, studies of chromate pigment production workers tended to show elevated risks of lung cancer in nearly all the cohorts and sub-cohorts reported, though not every relative risk estimate was statistically significantly increased.

Also, among chromium electroplating workers, there was a clear pattern of excess risk in most cohorts.

Workers in other industries who may have had somewhat lower levels of chromium VI exposure than those in the previously mentioned industries, had a less convincing set of relative risk estimates, though nearly all were above 1.0.

A few of the cohort studies collected high-quality data on smoking histories and incorporated these into nested case-control analyses; these tended to show elevated risks independent of smoking, and when smoking was adjusted for the relative risk of chromium VI exposure was increased. Many of the epidemiological studies were limited by co-exposures to other occupational lung carcinogens (e.g. certain other metals, asbestos) and a lack of adjustment for these and for smoking.

3.6 Asbestos and Lung Cancer

Our search focussing on terms related to the exposure circumstances of the presently prescribed diseases resulted in the identification of 26 relevant studies published since 2009 (i.e., the latest year for which the most recent IARC monograph had included studies). Nearly two thirds of the studies (17/26; 65%) pertained to asbestos mining or textile industries. Most of these studies were from China or USA, with significant overlap of participants within these sectors in each country. The remaining 9 studies mainly took place in Europe, covering shipbuilding, naval workers, and a mix of other occupations.

It is noteworthy that none of the identified studies took place in the UK. Since the search terms were based on the current prescriptions (to achieve a more manageable list of studies to review given resource and timeline constraints), it would be expected that the results would predominantly address these industries. There were also studies relating to mining exposure, but this was not relevant for occupational exposures in the UK.

The main results from each study indicated clear increases in lung cancer risks with asbestos exposure. Only four studies distinguished between lung cancer rates in those with asbestosis (though not in asbestosis-free individuals). A cohort study indicated lung cancer rates were more than doubled in individuals with asbestosis, and a case-control study found asbestosis rates were twice as high in cases compared to controls. Another one of the studies quantified very high risks of lung cancer in those with asbestosis. Based on this limited evidence, it was not possible to estimate lung cancer risk levels in those without asbestosis from different occupational exposure scenarios.

It is worth noting that there is now statistical evidence that there is a multiplicative interaction between smoking and asbestos exposure on lung cancer risk, with no requirement for asbestosis. In addition, the earlier Helsinki criteria for diagnosis of asbestos and asbestos-related cancer states that “A cumulative exposure of 25 fibre-years is estimated to increase the risk of lung cancer 2-fold, clinical cases of asbestosis may occur at comparable cumulative exposures.

Our updated search of occupational exposure to asbestos and lung cancer studies since 2009, based on the current prescriptions, identified 26 studies. Most of the search results were cohort studies (24), with the remaining using a case-control design (2). Overall, the studies identified since the most recent IARC report continued to indicate strong lung cancer risks with occupational exposure to asbestos, with the possible exception of the removal of the requirement for job history information in the presence of asbestosis in PD D8. From this review, there was no

evidence base to recommend revisions to the current IIAC prescription. However, there may be additional occupational circumstances with relevance to the UK, which could be examined in a broader review of the literature: for example, studies of lung cancer risks in construction workers, naval personnel, and vehicle mechanics, etc. Risk levels in these occupations from our search did appear to be lower than those currently prescribed, but nevertheless, a broadened search focussing on specific occupational exposures may be warranted and could be guided by the job categories that are known to be at increased risk of mesothelioma and/or asbestosis. Alternatively, a review of exposure studies could identify specific occupational circumstances whereby exposure to asbestos is likely to be associated with an RR>2.

4 Conclusions

The relevant current prescriptions are contained in the Appendix.

The relevant occupational epidemiological evidence for silica and COPD has been summarised, and based on this review alone it is not possible to recommend prescription in relation to silica and COPD in occupational circumstances covered by this review. However, there are two sets of occupational circumstances that seem worthy of further consideration by searching for studies in relevant occupations and industries, not just studies informative about silica exposure. These are foundry workers and construction workers, and it may be appropriate for IIAC to consider doing this as a matter of priority, noting that there are potentially other risk factors relevant for COPD in these industrial settings. It is possible that there are other occupational circumstances where silica exposures are relatively high (e.g. manufacture or installation of kitchen worktops) and we would suggest that IIAC also considers these.

We have summarised the relevant epidemiological literature for occupational exposure to silica and lung cancer. Based on this review, we think several occupational circumstances are worthy of further examination for evidence of a doubled relative risk. These are coal miners (where there is evidence of silica exposure from sandstone), quarry workers, and sand and gravel workers. However, because our searches focussed on silica exposure, it is possible that some occupational groups such as stonemasons will not have been picked up. Thus, we recommend that further literature searches for these specific industries are carried out before final conclusions are drawn.

Overall, the occupational epidemiological evidence for cleaning products and COPD is limited, but suggestive of increased risks. Based on this review alone, there is insufficient evidence to recommend prescription for additional occupational circumstances for COPD. Nevertheless, given the consistent risks apparent in the available evidence, there are likely to be studies published in the near future with larger sample sizes and more rigorous exposure assessment methods. We recommend that IIAC continues to monitor this literature base as a matter of priority.

Overall, the occupational epidemiological evidence for agricultural exposures and COPD is limited, but there is some evidence of increased risks, with two recent reviews reporting pooled ORs for COPD of 1.4 for occupational exposure to pesticides and 1.8 for farmers. Of the eight papers which are included, four investigated differences in agricultural exposure within groups of farmers, and four compared farmers to other occupational groups. Three of the four studies in this latter group were based on small numbers of farmers (20-30 individuals) so conclusions from these are limited; nonetheless two of these studies reported significantly increased risks of COPD with ORs > 2.0. The fourth study, which had a relatively larger study group but small numbers of cases of COPD did not find a significantly increased risk. A cohort study of over 1,000 farmers in Iowa, US found a significantly elevated OR=2.2 for airflow obstruction among farmers working with hogs or chickens in confined environments. Based on this review alone, there is currently insufficient evidence of a doubling of the relative risk to recommend prescription for additional occupational circumstances for COPD, however more data are developing in this area, and an updated review in the relatively short-term would be beneficial. As noted above, this review did not focus on the impacts of exposure to organic dusts or other potential agricultural exposures including bacteria, spores or gases. Thus, it would also be beneficial to carry out review of the association between COPD and these more specific exposures. In addition, exposures to allergens on farms, such as grain dust, have been associated with respiratory disease other than COPD (e.g. asthma, reduced lung function, 'farmers lung'). Further investigation of these other health outcomes would complement the findings of this report.

Chromate production workers have been at increased relative risk of lung cancer, which are more than doubled. However, it may be possible than this risk has decreased in more recent years. It is not clear from the current prescription if exposure to "zinc chromate, calcium chromate and strontium chromate in their pure forms" adequately cover chromate production work (in the UK), particularly in the earlier years of operation. From the epidemiological

evidence there is no reason to differentiate between different chromium salts or require them to be in a pure state. There is a suggestion from the literature that the relative risks of lung cancer in this industry are reduced after a certain date potentially to a level below 2, possibly from the 1980s onwards. This could usefully be further clarified, taking into account latency, perhaps in consultation with the industry. Smoking data were not always available and when present were highly variable, and not based on the ideal assessment of cumulative pack-years. However, where smoking was adjusted for there often remained an excess lung cancer risk due to hexavalent chromium. IIAC has previously examined the relative risks of lung cancer (due to chromium and other exposures) in chrome plating and certain forms of welding. It may be worth revisiting these issues to see if there is now any robust evidence of a doubling of the relative risk. Another industry worth examining for historic risks is cement production, although as for chromate production, this risk may have been removed or diminished due to changes in the production process. Finally given that IARC has classified work as a painter as definitely carcinogenic, it may be useful for IIAC to see to what extent there might be an increased risk among painters who used chrome-based paints.

The majority of studies of asbestos and lung cancer examined the textile and mining industries, with the others involving shipbuilding, navy personnel, insulation workers, vehicle mechanics, and other occupations. The studies demonstrated substantially elevated lung cancer risks in those occupationally exposed to asbestos, with limited evidence differentiating risk levels only in those with asbestosis. While there is no clear rationale to revise the current IIAC prescription definitions for lung cancer and asbestos exposure, apart perhaps from specific occupational circumstances in the presence of asbestosis), a broader search including other occupational circumstances involving asbestos exposure may be warranted in order to ensure that there are no other groups of asbestos exposed workers with lung cancer currently being excluded by the current prescription. Alternatively, a review of exposure studies could identify specific occupational circumstances whereby exposure to asbestos is likely to be associated with an RR>2.

Appendix- Relevant current prescriptions

Disease Number	Name of Disease or Injury	Type of job
	Miscellaneous conditions not included elsewhere in the list	**Any job involving**
D12	Chronic obstructive pulmonary disease – COPD where, with maximum effort, where there is evidence of a forced expiratory volume in one second which is: (i) at least one litre below the appropriate mean value predicted, obtained from the following prediction formulae which give the mean values predicted in litres: 1. For a man, where the measurement is made without back-extrapolation, (3.62 x Height in metres) minus (0.031 x Age in years) minus 1.41; or, where the measurement is made with back-extrapolation, (3.71 x Height in metres) minus (0.032 x Age in years) minus 1.44 2. For a woman, where the measurement is made without back-extrapolation, (3.29 x Height in metres) minus (0.029 x Age in years) minus 1.42; or, where the measurement is made with back-extrapolation, (3.37 x Height in metres) minus (0.030 x Age in years) minus 1.46 or (ii) less than one litre.	Exposure to coal dust (whether before or after 5th July 1948) by reason of working– (a) underground in a coal mine for a period or periods amounting in aggregate to at least 20 years; (b) on the surface of a coal mine as a screen worker for a period or periods amounting in aggregate to at least 40 years before 1st January 1983; or (c) both underground in a coal mine, and on the surface as a screen worker before 1st January 1983, where 2 years working as a surface screen worker is equivalent to 1 year working underground, amounting in aggregate to at least the equivalent of 20 years underground. Any such period or periods shall include a period or periods of incapacity while engaged in such an occupation.

D11	Primary carcinoma of the lung where there is accompanying silicosis.	Exposure to silica dust in the course of: (a) the manufacture of glass or pottery (b) tunnelling in, or quarrying sandstone or granite (c) mining metal ores (d) slate quarrying or the manufacturing of artefacts from slate. (e) mining clay (f) using siliceous materials as abrasives (g) cutting stone (h) stonemasonry (i) work in a foundry.

Disease Number	Name of Disease or Injury	Type of job
	Miscellaneous conditions not included elsewhere in the list	**Any job involving**
D12	Chronic obstructive pulmonary disease – COPD where, with maximum effort, where there is evidence of a forced expiratory volume in one second which is: (i) at least one litre below the appropriate mean value predicted, obtained from the following prediction formulae which give the mean values predicted in litres: 3. For a man, where the measurement is made without back-extrapolation, (3.62 x Height in metres) minus (0.031 x Age in years) minus 1.41; or, where the measurement is made with back-extrapolation, (3.71 x Height in metres) minus (0.032 x Age in years) minus 1.44 4. For a woman, where the measurement is made without back-extrapolation, (3.29 x Height in metres) minus (0.029 x Age in years) minus 1.42; or, where the measurement is made with back-extrapolation, (3.37 x Height in metres) minus (0.030 x Age in years) minus 1.46 or (ii) less than one litre.	Exposure to coal dust (whether before or after 5th July 1948) by reason of working– (d) underground in a coal mine for a period or periods amounting in aggregate to at least 20 years; (e) on the surface of a coal mine as a screen worker for a period or periods amounting in aggregate to at least 40 years before 1st January 1983; or (f) both underground in a coal mine, and on the surface as a screen worker before 1st January 1983, where 2 years working as a surface screen worker is equivalent to 1 year working underground, amounting in aggregate to at least the equivalent of 20 years underground. Any such period or periods shall include a period or periods of incapacity while engaged in such an occupation.

C18	Emphysema	Inhalation of cadmium fumes for a period of, or periods which amount in aggregate to, 20 years or more.

Primary carcinoma of the lung.	Exposure to zinc chromate, calcium chromate or strontium chromate in their pure forms
D8. Primary carcinoma of the lung where there is accompanying evidence of asbestosis.	(*a*) The working or handling of asbestos or any admixture of asbestos; or (*b*) the manufacture or repair of asbestos textiles or other articles containing or composed of asbestos; or (*c*) the cleaning of any machinery or plant used in any of the foregoing operations and of any chambers, fixtures and appliances for the collection of asbestos dust; or (*d*) substantial exposure to the dust arising from any of the foregoing operations.
D8A. Primary carcinoma of the lung.	Exposure to asbestos in the course of— *(a)* the manufacture of asbestos textiles; or *(b)* spraying asbestos; or *(c)* asbestos insulation work; or *(d)* applying or removing materials containing asbestos in the course of shipbuilding, where all or any of the exposure occurs before 1st January 1975, for a period of, or periods which amount in aggregate to, five years or more, or otherwise, for a period of, or periods which amount in aggregate to, ten years or more.

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