MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HĪKINA WHAKATUTUKI

COVERSHEET

Minister	Hon Matt Doocey	**Portfolio**	ACC
Title of Cabinet paper	Seeking Feedback on Recommended Additions to Schedule 2, List of Occupational Diseases – Approval to Consult	**Date to be published**	20 December 2024

List of documents that have been proactively released		
Date	**Title**	**Owner**
28 November 2023	*Occupational Diseases Review for Schedule 2 of the Accident Compensation Act 2001*	MBIE

Information redacted **YES / NO** *(please select)*

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Occupational Diseases Review

For Schedule 2 of the Accident Compensation Act 2001

28 November 2023

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Dr Chris Walls

Professor David McBride

Associate Professor Deborah Read.

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Executive summary

In 2023, *Allen + Clarke* conducted a review of Schedule 2 of the Accident Compensation Act 2001 (Schedule 2) to determine if there is sufficient evidence to support the addition of further specific exposure/disease pairings. Key documents that informed the scope of this review were the International Labor Organisation (ILO) Occupational Diseases List, the Australian Deemed Diseases List, and the Summary of Public Submissions collected from Ministry of Business, Innovation and Employment's (MBIE) public consultation in April 2023 on the current Schedule 2 update.

Allen + Clarke triaged the substantial number of potentially eligible diseases and exposures, followed an assessment by the Independent Panel (the Independent Panel), which informed a series of evidence reviews. The Independent Panel reviewed both published, peer-reviewed and grey literature, and made recommendations based on this evidence and their clinical experience and expertise. Recommendations were determined against a set of criteria agreed by the Cabinet.

Removal of diseases from the current Schedule 2 list was not within the scope of this review.

This report summarises the work completed to date including the evidence review findings. It serves as the Independent Panel's recommendations to MBIE on the exposure/disease pairings that the Independent Panel recommends be included in the refreshed iteration of Schedule 2.

The Independent Panel recommends that the following exposure/disease pairings be included on Schedule 2 of the Accident Compensation Act (2001) because there is sufficient evidence of causality to warrant automatic acceptance of a work-related Schedule 2 claim:

- 1,2-Dichloropropane and cholangiocarcinoma
- Ammonia and chronic corneal ulcer
- Asbestos and laryngeal cancer
- Asbestos and ovarian cancer
- Butadiene and leukaemia
- Erionite and malignant mesothelioma
- Firefighting and bladder cancer
- Firefighting and mesothelioma
- Infrared radiation and heat-induced cataracts (glassblowers' disease)
- Nickel and nasal cancer
- Potroom emissions and asthma
- Trichloroethylene and kidney cancer
- Vinyl chloride and hepatocellular carcinoma
- Welding and ocular melanoma
- Cover for future pandemics.

There is insufficient evidence of causality to warrant automatic acceptance of a work-related Schedule 2 claim for the following exposure/disease pairings. These work-related injury or gradual process injuries for the following would be better addressed through another ACC type of claim, such as a work-related gradual process claim, rather than Schedule 2.

- Acrylonitrile and cancer
- Alcohol, glycols or ketones and diseases

- Aluminium and aluminosis, bauxite fibrosis (Shaver's disease) and chronic obstructive pulmonary disease (COPD)
- Ammonia and COPD and pulmonary fibrosis
- Antimony or its compounds and nose septal ulceration, deposits on teeth or antimoniosis
- Benzoquinone and vitiligo
- Cadmium (or its compounds) and kidney cancer, and pulmonary emphysema, ansomia, osteoporosis, osteomalacia, itai-itai, Fanconi disease, and nephropathy
- Carbon disulphide and chronic toxic encephalopathy, toxic optical neuropathy, ototoxic hearing loss, atherosclerosis, chronic ischaemic heart disease, secondary hypertension and chronic kidney disease
- Chlorine and COPD, emphysema, chronic bronchiolitis, pulmonary fibrosis, chronic rhinitis and erosion of the teeth
- Coal tar and pitches and bladder cancer and renal cancer
- Copper and hepatic granuloma, chronic pulmonary fibrosis and chalcosis
- Cyclophosphamide and leukaemia
- Fluorine and dental fluorosis, skeletal fluorosis and COPD
- Food flavourings and obliterative bronchiolitis
- Formaldehyde and leukaemia
- Hard metal dust and sensitizer-induced occupational asthma and hard metal lung disease
- Irritant and allergic dermatitis for any exposure
- Isocyanates and allergic rhinitis, allergic conjunctivitis and COPD
- Lindane and non-Hodgkin's lymphoma (NHL)
- Methyl ethel ketone and chronic toxic encephalopathy
- Methyl isobutyl ketone and polyneuropathy
- Mineral acids and nasal septal ulceration and laryngeal cancer
- Nail technician and respiratory diseases
- Nickel (or its compounds) and asthma
- Nitroglycerin and chronic toxic encephalopathy, angina pectoris and Raynaud's phenomenon
- Non-fibrogenic mineral dust and stannosis, baritosis, pneumoconiosis due to titanium dioxide and antimoniosis
- Optical radiations and chronic blepharoconjunctivitis, and actinic cataracts
- Oxides of nitrogen or its compounds and bronchiolitis obliterans, COPD and B12 deficiency
- Pentachlorophenol (PCP) and NHL
- Pesticides and anti-coagulation syndrome due to exposure to coumarin derivatives, toxic effects caused by pentachlorophenol and carcinogenic effects of pesticides
- Pharmaceutical agents and carcinogenic effects of antineoplastic drugs
- Platinum (or its compounds) sensitiser asthma
- Platinum and allergic rhinitis and allergic urticaria
- Polychlorinated biphenyl and malignant melanoma
- Polycyclic aromatic hydrocarbons and lung cancer, non-melanoma skin cancers
- Selenium and selenosis
- Sulphur oxides and chronic skin and mucous membranes irritation, nose septal ulceration, COPD, chronic bronchiolitis obliterans, emphysema and pulmonary fibrosis
- Thallium and polyneuropathy
- Vanadium (or its compounds) and asthma.

Diseases & Exposures Recommended for Inclusion on Schedule 2

The following disease and exposure pairs have been recommended by the Panel for inclusion to Schedule 2 of the Accident Compensation Act (2001).

1,2-Dichloropropane & Cholangiocarcinoma	Ammonia & Chronic Corneal Ulcer	Asbestos & Laryngeal Cancer
Asbestos & Ovarian Cancer	Butadiene & Leukaemia	Erionite & Malignant Mesothelioma
Firefighting & Bladder Cancer	Firefighting & Mesothelioma	Infrared Radiation & Heat-Induced Cataracts (Glassblowers' Disease)
Nickel & Nasal Cancer	Potoom Emissions & Asthma	Trichloroethylene & Kidney Cancer
Vinyl Chloride & Hepatocellular Carcinoma	Welding & Ocular Melanoma	

1 Introduction

A person in Aotearoa New Zealand can access Accident Compensation Corporation (ACC) cover for the work-related gradual process, disease, or infection injuries listed in Schedule 2 of the Accident Compensation Act 2001 (the AC Act). The Schedule 2 list complements a general cover provision in section 30(2) and (2A) of the AC Act, which provides cover for claims that meet a set of defined criteria. Schedule 2 provides a simpler pathway to cover for specified occupational diseases where there is sufficient evidence of causality to warrant automatic acceptance of a work-related claim. Schedule 2 was last updated in 2008. Reviewing Schedule 2 now will ensure that it reflects recent scientific evidence of causal links between specific work-related exposure/disease pairings.

The Accident Compensation Policy team at the Ministry for Business, Innovation and Employment (MBIE) contracted *Allen + Clarke* to review potential additions to Schedule 2 of the AC Act. MBIE required a literature review of work-related causality and specified occupational diseases (triaged by *Allen + Clarke*) and the establishment and management of an independent Panel of medically qualified experts to analyse the literature findings against technical criteria and a report that makes recommendations about changes to Schedule 2. MBIE will use this information to inform recommendations to the Minister for ACC on proposed changes to Schedule 2.

1.1 Purpose and methodology

This purpose of this report is to set out the evidence review summaries for each of the diseases (by exposure) that were reviewed for potential inclusion in Schedule 2 of the AC Act 2001. It describes the independent Panel's deliberations on each exposure/disease pairing in relation to whether there is sufficient evidence of causality to enable automatic acceptance of a claim under Schedule 2. Recommendations align with the technical criteria as agreed by the Cabinet.

Removal of diseases from the current Schedule 2 list, or amendment of the structure of Schedule 2, is not within the scope of this review.

The methodology section below summarises the methodology used to prepare this report, including the technical criteria for assessing exposure/disease pairings in relation to the purpose of Schedule 2, sources of information informing the review, our triaging process and evidence review strategy.

1.1.1 Technical criteria and the decision-making framework

The technical criteria (as agreed to by Cabinet) are set out below. These criteria are informed by the Austin Bradford Hill assessment criteria and were the basis for the Independent Panel's deliberations.

Strength of association: The greater the impact of an exposure on the occurrence or development of a disease, the stronger the likelihood of a causal relationship.

Consistency or reproducibility: Consistent findings observed by different persons in different places with different samples strengthen the likelihood of an effect.

Specificity: Causation is likely if there is a very specific population at a specific site and disease with no other likely explanation. The more specific an association between a factor and an effect is, the bigger the probability of a causal relationship.

Temporality or time sequence: The effect has to occur after the cause (and if there is an expected delay between the cause and expected effect, then the effect must occur after that delay).

Biological gradient: Greater exposure should generally lead to greater incidence of the effect; however, in some cases, the mere presence of the factor can trigger the effect. In other cases, an inverse proportion is observed: greater exposure leads to lower incidence.

Biological plausibility: From what is known of toxicology, chemistry, physical properties, or other attributes of the studied risk or hazard, it makes biological sense to suggest that exposure leads to the disease or injury.

Coherence: A general synthesis of all the evidence (eg, human epidemiology and animal studies) leads to the conclusion that there is a cause-effect relationship in a broad sense and in terms of general common sense.

Analogy: The use of analogies or similarities between the observed association and any other associations.

Experimental evidence: This can be considered if relevant.

The technical criteria were used to establish if the causal connection between the diseases and work-related exposure is sufficiently strong to enable automatic acceptance of a claim under Schedule 2. These were agreed by the Cabinet and are:

Insufficient causal evidence: Diseases will be excluded if evidence of the causal connection between the disorder and employment is not sufficiently strong to allow a connection to work to be automatically accepted.

'Sufficiently strong' here is not generally quantifiable. For each condition on Schedule 2 it will need to be based on an expert assessment of the evidence available and its quality.

Proportion of work cases: Diseases will only be included if employment is the cause of the disorder in a significant majority of the cases of that disorder in a subset of the population, identified based on the subset's exposure to particular work tasks, or particular work environments.

1.1.2 Sources of exposure/disease pairings

MBIE requested that this review of Schedule 2 assessed three sources of diseases and exposure that could potentially be added to Schedule 2:

- The ILO List[1]
- Australia's Deemed Diseases List[2]
- A list of diseases raise by submitters during the 2023 public consultation on the Schedule 2 review.[3]

Allen + Clarke used these three documents as the primary sources for exposure/disease pairings to consider as part of the evidence review process.

ILO methodology

The ILO List is a comprehensive report detailing a list of related occupational exposure/disease pairings, as well as detail on exposure routes, latency periods and other background information. It provided much of the background analysis in preparation for the

evidence reviews and Independent Panel discussions. This information has, in many cases throughout this report, been supported by other published peer-reviewed literature findings.

The ILO note in its methodology that the criteria used by its experts for deciding what specific diseases be considered in the updated list include that:

- there is a causal relationship with a specific agent, exposure, or work process
- they occur in connection with a specific work environment and/or in specific occupations
- they occur among the groups of workers concerned with a frequency which exceeds the average incidence within the general population
- there is scientific evidence of a clearly defined pattern of disease following a work-related exposure and plausibility of cause.[1]

For the relevant ILO exposure/disease pairings, *Allen + Clarke* reviewed the ILO's data, including the bibliographic details, which allowed us to determine the dates of the relevant research used by the ILO. These dates were used as a proxy to inform the searches for the 2023 Aotearoa New Zealand evidence reviews presented in this paper. Detailed search methodologies were not provided by the ILO for each exposure category, as it would have been impractical to do so given the substantial number of exposure/disease pairings. We were not able to replicate their search strategies.

Deemed Diseases methodology

The original recommended DD List (developed by Safe Work Australia) was based on a review of the literature up to the end of 2014. An updated DD List was released in 2021, with contributing evidence reviews covering the period 2015 up to July 2021. For a small number of diseases, some literature published prior to 2015 was also considered.

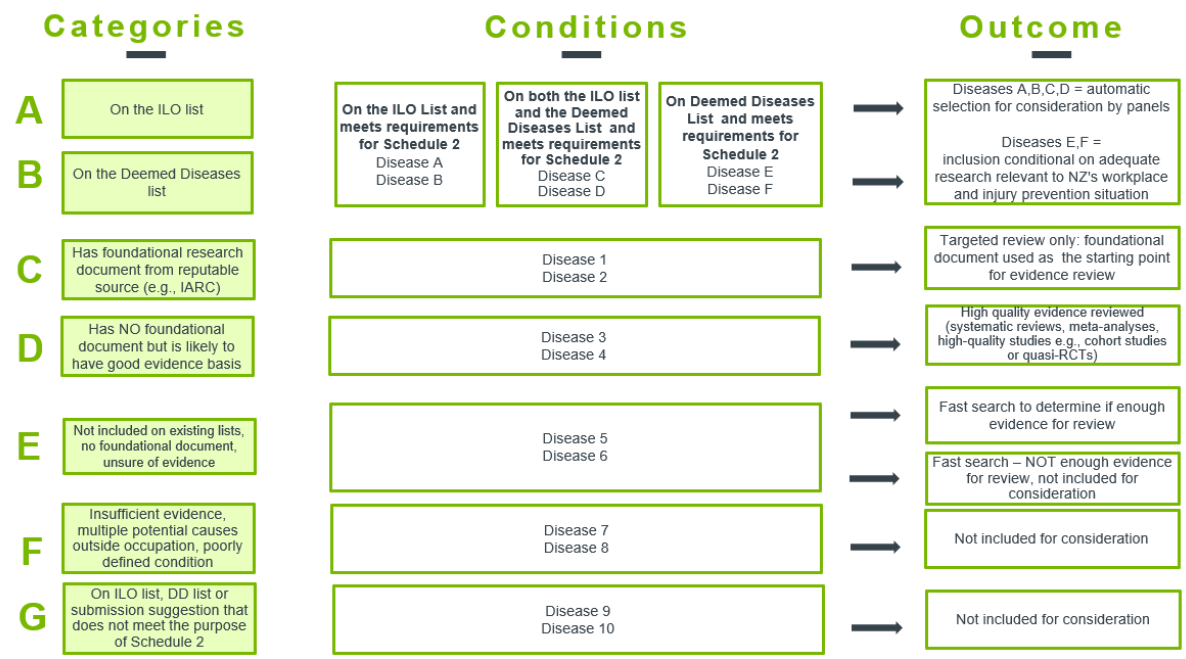
Relevant key words for each of the diseases and exposures were paired with ['occupation*' OR 'work-related*]. For cancers, the classifications in the IARC Monographs were used, with only exposures classified as Group 1 (definite human carcinogens) included, paired only with cancers for which IARC considered there was sufficient evidence of causation.[4]

For the relevant DD List exposure/disease pairings, *Allen + Clarke* reviewed the information presented in detail, to extract relevant information. As the search dates were given as concluding in July 2021, this was the proxy date used to inform the searched for evidence presented in this paper.

1.1.3 Triaging process

As there were several hundred exposure/disease pairings that could potentially be included across the three sources, *Allen + Clarke* developed a comprehensive three-step triaging process (agreed with MBIE). The purpose was to ensure that only those exposure/disease pairings that could potentially meet the purpose of Schedule 2 were reviewed in detail by the independent Panel. Our approach was informed by a preliminary review of exposure/disease pairings suggested in the three sources against the list of occupational diseases currently in Schedule 2 of the AC Act 2001. We created the following triage framework to ensure a robust and transparent analysis of exposure/disease pairings that should be considered for inclusion in Schedule 2 and where further evidence review and Independent Panel consideration/recommendations were required.

Step one of the triaging process involved sorting exposure/disease pairings for the three sources into seven categories, as detailed below.



Categories A + B: ILO and Deemed Diseases

Categories A + B included the exposure/disease pairings that appeared on the ILO or DD List (or both). These were checked against Schedule 2 to remove items that were already covered. *Allen + Clarke* discussed the triage approach with MBIE to determine which exposure/disease pairings required further evidence review, with these being considered by the Independent Panel. It was assumed that in order for the ILO or DD List to publish a causational link between a work-related exposure and a disease, relevant evidence would have been evaluated in an expert-led processes.

Category C: Foundational international authority research document available

Category C covered exposure/disease pairings that were suggested by submitters in the 2023 public consultation round and linked to a foundational research document by a credible authority. Diseases in this category were further investigated, initially through the foundational document, with other high-quality research (good quality systematic reviews with meta-analysis, RCTs/quasi-RCTs or large cohort studies with adequate control for bias and confounding) sought where necessary.

Category D: No foundational document, good evidence

Category D covered exposure/disease pairings that were suggested by submitters in MBIE's 2023 public consultation on the occupational diseases review, but for which *Allen + Clarke* was unable to identify a foundational document from a credible and scientific authority. Applying clinical knowledge, we assumed that for these diseases there may be high-quality evidence such as good quality systematic reviews with meta-analysis, RCTs/quasi-RCTs, large cohort studies with adequate control for bias and confounding, or case-control studies (for rare diseases).

Category E: No foundational document, unclear evidence

Category E covered exposure/disease pairings that were suggested by submitters in the 2023 public consultation round but the diseases were not included on the ILO List or the DD List, there was no foundational document from a credible, scientific authority and the depth and breadth of the potential evidence base was unclear. *Allen + Clarke* conducted a search of agreed sources (PubMed and Cochrane) to determine if there was sufficient high-quality

evidence for these diseases to be reviewed in more detail. Those that had sufficient evidence to warrant review were transferred to Category D.

Category F: Insufficient evidence

Category F exposure/disease pairings were suggested in the Summary of Submissions but were not on either ILO or DD list, did not have a foundational research document and did not appear to have clear biological plausibility or strong research investigating causality. In addition, Category F also included exposure/disease pairings that were not sufficiently well defined (such as not having a relevant ICD code or being very broadly defined). Evidence on work-related causality was not investigated.

Category G: On Submission suggestions list, ILO list or DD list that does not meet the purpose of Schedule 2: no further work will be completed on this group

Category G acknowledged that there are exposure/disease pairings listed on the ILO list, the DD list and in the Submissions Summary suggestion list that do not meet the purpose of Schedule 2. Evidence on work-related causality for these diseases was not investigated.

1.1.4 Evidence search, selection, and review

Search strategy

Specific search strategies are available on request.

After discussion and confirmation with the Independent Panel to confirm the PICO(T/S), *Allen + Clarke* completed the search of the agreed databases:

- PubMed
- Clinialtrials.gov
- Cochrane Library database.

We reviewed the websites of the following reputable international authorities to identify any peak body publications, technical reports and monographs of relevance to the exposure/disease pairings triaged A to E.

- International Agency for Research on Cancer (**www.iarc.who.int**)
- International Labour Organization (**www.ilo.org**)
- Institute of Medicine (**www.iom.edu**)
- Centers for Disease Control and Prevention (**www.cdc.gov**) and the National Institute for Occupational health and Safety (NIOSH) (**www.cdc.gov/niosh**) .

The last literature searches were conducted on 30 October 2023.

Bibliographies of included studies were reviewed for additional papers that met the PICO(T/S).

Study selection

Inclusion criteria were:

- applicability to the PICO(T/S) including meeting the agreed date ranges (built on the publication date of the relevant formative document(s) prepared by independent and credible international bodies like IARC, IOM, NIOSH, and the ILO)
- sufficient statistical data about causality to enable consideration by the Independent Panel
- English-language, full text paper available.

Papers were excluded if they:

- did not include sufficient description of an exposure that was clearly related to a workplace environment
- did not meet the agreed inclusion criteria (above)
- were guidelines, commentary, opinion pieces, conference abstracts, oral presentations or poster presentations not accompanied by a full academic paper
- were a duplicate study, a study with an overlapping or duplicate dataset (the largest and more comprehensive dataset was selected in these cases)
- original research was a contributing paper to a larger, high-quality systematic review.

Studies were reviewed by two *Allen + Clarke* project team members with technical oversight and review provided by the independent Panel and our clinical advisor (Dr Mary Obele). Zotero was used as the preferred citation management system. Citation data, study type, country, number of study participants (cases/controls), results including effect size, any covariates and adjustment for confounding, bias, and author conclusions about causality were assessed.

Quality assessment

Studies were assessed for relevance by two analysts reviewing titles and abstracts and one analyst reviewing full text papers. A **SIGN**-style assessment was conducted to ensure quality for all papers reviewed. This is available on request.

No independent statistical analysis or meta-analysis was completed.

No GRADE assessment was completed.

Results

The total number of academic sources included in this literature review, following exclusions, was 22 papers: 9 meta-analyses, 7 systematic reviews, 3 cross-sectional, 2 cohort studies and 1 trial.

Once reviewed and appraised, each included study was written up (study description, notes on the strength of the study and its findings, key findings data as relevant to the research question), and the findings are included in section 3 of this report.

1.1.5 The independent Panel

Allen + Clarke convened an independent Panel comprising of three members: Professor David McBride, Dr Chris Walls and Associate Professor Deborah Read. The independent Panel provided advice on the application of the technical criteria to the agreed list of potential diseases that could be added to Schedule 2. The Independent Panel is responsible for making recommendations about whether a disease should be added to Schedule 2 (or not) and for providing a rationale for its view in line with the technical criteria set by the Cabinet. Decisions were made by consensus.

The independent Panel met two times:

- Meeting 1 (10 October 2023):
  - Discussion of the triaging framework and process to date
  - Preliminary assessment of exposure/disease pairings eligible for consideration
  - Curation of a defined list of exposure/disease pairings for *Allen + Clarke* to conduct evidence reviews for.
- Meeting 2 (20 November 2023):
  - Discussion of evidence for exposure/disease pairings eligible for consideration
  - Decisions made on what exposure/disease pairs had sufficient evidence for recommended inclusion to Schedule 2

- Unanimous decisions from all Panel members, supported by views of Technical Expert Dr Mary Obele.

1.2 Limitations and considerations

For many of the evidence reviews, there was a significant lack of relevant evidence available. Where this is the case, it has been noted in the evidence review tables. There is substantial lack of occupational research conducted in Aotearoa New Zealand which has resulted in limited data availability for this review. This includes limited information about exposures. *Allen + Clarke* and the Independent Panel relied on data and analyses published internationally, which may have limited relevance to the Aotearoa New Zealand context. To mitigate this risk, *Allen + Clarke* sought advice from the Independent Panel on which exposures might be most relevant to Aotearoa New Zealand, based on their clinical experience and expertise. Additionally, *Allen + Clarke* requested data from ACC regarding the exposure/disease pairings, but none was able to be provided as it is not collected. We thank ACC for their support with this part of the work.

The review was approached with an intersectional and gender equity lens. There was little epidemiological evidence that specifically supported this lens, though we have identified some diseases and occupational exposures (such as formaldehyde and endometriosis, shift work and breast cancer) with emerging evidence that should be prioritised at the next review of Schedule 2.

2 Exposure/disease pairings considered by the Independent Panel

Section 2 of this report outlines the exposure/disease pairings as categorised through the triaging process, the evidence considered by the independent Panel and the assessment of the technical criteria set by the Cabinet. Given the substantial expertise of the Independent Panel, clear guidelines provided by MBIE, and the evidence provided by *Allen + Clarke*, the Independent Panel were able to make confident decisions about the exposure/disease pairings recommended for inclusion to Schedule 2 at this time.

2.1 Exposure/disease pairings recommended for addition to Schedule 2 with grey literature only

Section 2.1 describes the exposure/disease pairings that the Independent Panel determined did not require academic supporting evidence as the evidence provide by ILO, IARC, as well as the Independent Panel's clinical expertise was sufficient to determine causality and to complete the assessment against the technical criteria set by the Cabinet. These exposure/disease pairings have a known and well documented causational link. Included in this section are:

- **Ammonia and chronic corneal ulcer**
- **Erionite and malignant mesothelioma**
- **Infrared radiation and heat induced cataracts**
- **Nickel and nasal cancer**
- **Potroom emissions and asthma**
- **Welding and ocular melanoma**

2.1.1 Ammonia and chronic corneal ulcer

Evidence for the Independent Panel's review		
Exposure	Ammonia (gas and liquid forms)	
Related diseases	Chronic corneal ulcer	
Summary statement	Sufficient causal relationship based on clinical experience of the Independent Panel, supported by designation as an occupational exposure/disease pairing by the ILO.	
ILO guidance notes	Corneal ulcers caused by ammonia is listed. "Exposure to ammonia vapours causes irritation and caustic burns of several areas, including the eyes. The full extent of damage to the eyes may not be clear until up to one week after the injury. Occupational exposure occurs in the manufacture of agricultural fertilizers and the manufacture of organic chemicals. It is also used in the manufacture of dyes, pesticides, plastics, explosives, pharmaceuticals and other fine chemicals. It is commonly employed in the pulp and paper, food and beverage, textile, leather, and metallurgical industries."[1]	
IARC advice	Not relevant for this disease (not cancer).	
NIOSH advice	Ammonia is used in agricultural, industrial, mining, metallurgy, petroleum refining and commercial refrigeration industries.[5] Exposure routes include inhalation, ingestions and skin/eye contact. Relevant symptoms for corneal ulcer include eye burns and irritation.[6]	
Deemed Diseases List advice	Ammonia is included under occupational asthma. Chronic corneal ulcer is not listed.[4]	
Existing Schedule 2 entry	No relevant entry.	
Summary of Independent Panel's assessment		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on clinical experience, there is a strong association between occupational ammonia exposure and chronic corneal ulcer. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases* report.[1]
	Consistency or reproducibility	Based on clinical experience, there is a consistent association between occupational ammonia exposure and chronic corneal ulcer. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases* report.[1]

Evidence for the Independent Panel's review		
	Specificity	The relationship between ammonia exposure and chronic corneal ulcer is well defined.
	Temporality or time sequence	Corneal ulcers occur after ammonia exposure. For acute ulcer (not recommended) the minimum duration of exposure is a few seconds and latency period is hours to weeks.[1] However, as this is a chronic condition, exposure and latency may be longer in some cases.
	Biological gradient	Yes. There is a dose-response relationship between ammonia exposure and chronic corneal ulcer.[1]
	Biological plausibility	Yes. It is biologically plausible that ammonia can cause corneal ulcers.[1]
	Coherence	Synthesis of evidence presented by the ILO concludes that there is a cause-effect relationship between ammonia and chronic corneal ulcer.[1]
	Analogy	Unknown.
	Experimental evidence	Not relevant for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on clinical experience, and supported by the evidence presented by the ILO, there is sufficiently strong causal evidence linking occupational ammonia exposure and chronic corneal ulcer.
	Proportion of work cases	Accurate exposure data for ammonia and chronic corneal ulcer is not available for Aotearoa New Zealand at this time.
Independent Panel recommendation	**Recommend inclusion on Schedule 2 as there is a well-established and accepted relationship. No further evidence review required.**	
Suggested wording to incorporate into Schedule 2	Chronic corneal ulcer diagnosed caused by occupational exposure to ammonia.	

2.1.2 Erionite and malignant mesothelioma

Evidence for the Independent Panel's review		
Exposure	Erionite (solid organic fibres – exposure via inhalation of fibres)	
Related diseases	Malignant mesothelioma	
Summary statement	Sufficient causal relationship based on clinical experience of the Independent Panel, supported by designation as an occupational exposure/disease pairing by the ILO and IARC.	
ILO guidance notes	Mesothelioma caused by erionite is listed. "The most common site of mesothelioma is the pleura; however, mesothelioma of the peritoneum has also been observed in subjects exposed to erionite. The prognosis of malignant mesothelioma is generally very poor, and the survival from the diagnosis is usually less than 1.5 years, with estimated median survival time varying from 4 to 12 months."[1]	
IARC advice	There is sufficient evidence in humans for the carcinogenicity of erionite. Erionite causes mesothelioma.[7]	
NIOSH advice	NIOSH recognises erionite as an occupational hazard but has not published its own data or summary statement on erionite and malignant mesothelioma specifically.	
Deemed Diseases List advice	Mesothelioma caused by asbestos is listed, but mesothelioma caused by erionite is not.	
Existing Schedule 2 entry	Mesothelioma caused by asbestos is listed, but mesothelioma caused by erionite is not.	
Summary of Independent Panel's assessment		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on clinical experience, there is a strong association between occupational erionite exposure and mesothelioma. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases*[1] report, and IARC *Monographs Vol 100C.*[7]
	Consistency or reproducibility	Based on clinical experience, there is a consistent association between occupational erionite exposure and mesothelioma. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases*[1] report and IARC *Monographs Vol 100C.*[7]
	Specificity	The relationship between erionite and mesothelioma is well defined.

Evidence for the Independent Panel's review		
	Temporality or time sequence	Mesothelioma occurs after erionite exposure. Exposure duration and latency period are not specified by the ILO or IARC.
	Biological gradient	Yes. There is a dose-response relationship between erionite and mesothelioma.[1,7]
	Biological plausibility	Yes. It is biologically plausible that erionite can cause mesothelioma.[1,7]
	Coherence	Synthesis of evidence presented by the ILO and IARC concludes that there is a cause-effect relationship between erionite exposure and mesothelioma.[1]
	Analogy	Erionite is a zeolite, which has similarities to asbestos (asbestos and zeolites are silicate-based minerals, linked inextricably via paradoxical similarities and differences which have emanated from different geological epochs).[8] Asbestos is an accepted cause of mesothelioma, as listed on Schedule 2.
	Experimental evidence	Not relevant for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on clinical experience and supported by the evidence presented by the ILO and IARC, there is sufficiently strong causal evidence linking erionite exposure and mesothelioma.
	Proportion of work cases	Accurate exposure data for erionite and mesothelioma is not available for Aotearoa New Zealand at this time.
Independent Panel recommendation	**Recommend inclusion on Schedule 2 as there is a well-established and accepted relationship. No further evidence review required.**	
Suggested wording to incorporate into Schedule 2	Mesothelioma diagnosed caused by occupational exposure to erionite.	

2.1.3 Infrared radiation and heat-induced cataracts (glass blowers' disease)

Evidence for the Independent Panel's review		
Exposure	Infrared radiation	
Related diseases	Heat-induced cataract (glass blowers' disease)	
Summary statement	Sufficient causal relationship based on clinical experience of the Independent Panel, supported by designation as an occupational exposure/disease pair by the ILO.	
ILO guidance notes	Glass blowers' diseases caused by infrared radiation is listed. "This disease typically occurs among those working in the occupation of glassblowing. Other occupational groups at risk are furnace, molten glass/metals workers, foundry workers or blacksmiths. Chronic exposure to infrared radiation emitted from heating of glass or molten metal is the very likely cause of the disease. Consequent to absorption of infrared radiation by the iris and lens of the eye, there is a probable increase in temperature and protein denaturation in the lens. Damage of the tissues appears as irregularly shaped opacification forms at the posterior cortex of the lens, and that leads to blurring of vision. The severity of the damage depends on the cumulative dose."[1]	
IARC advice	Not relevant for this disease (not cancer).	
NIOSH advice	Infrared radiation has long been associated with cataracts. Cataracts may be produced by prolonged exposure to wavelengths that may not burn the skin.[9]	
Deemed Diseases List advice	Neither infrared radiation nor glassblowers' disease/heat-induced cataracts are listed.	
Existing Schedule 2 entry	No relevant entry.	
Summary of Independent Panel's assessment		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on clinical experience, there is a strong association between occupational infrared radiation exposure and heat-induced cataracts. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases* report.[1]
	Consistency or reproducibility	Based on clinical experience, there is a consistent association between occupational infrared radiation exposure and heat-induced cataracts. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases* report.[1]

Evidence for the Independent Panel's review		
	Specificity	The relationship between infrared radiation exposure and heat-induced cataracts is well defined.
	Temporality or time sequence	Heat-induced cataracts occur after infrared radiation exposure. The minimum duration of exposure is one year and maximum latency period is 15 years.[1]
	Biological gradient	Yes. There is a dose-response relationship between heat induced cataracts and infrared radiation.[1]
	Biological plausibility	Yes. It is biologically plausible that infrared radiation can cause cataracts.[1]
	Coherence	Synthesis of evidence presented by the ILO concludes that there is a cause-effect relationship between infrared radiation exposure and heat-induced cataracts.[1]
	Analogy	Unknown for this diseases/exposure pairing.
	Experimental evidence	Not relevant for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on clinical experience, and supported by the evidence presented by the ILO, there is sufficiently strong causal evidence linking infrared radiation exposure and heat-induced cataracts.
	Proportion of work cases	Accurate exposure data for infrared radiation and heat-induced cataracts is not available for Aotearoa New Zealand at this time.
Independent Panel recommendation	**Recommend inclusion on Schedule 2 as there is a well-established and accepted relationship. No further evidence review required.**	
Suggested wording to incorporate into Schedule 2	New entry: Heat-induced cataracts (also known as glass-blowers disease) of the eye diagnosed caused by occupational exposure to infrared radiation.	

2.1.4 Nickel and nasal cancer

Evidence for the Independent Panel's review		
Exposure	Nickel (fumes, dusts, and mists)	
Related diseases	Nasal cancer	
Summary statement	Sufficient causal relationship based on clinical experience of the Independent Panel, supported by designation as an occupational exposure/disease pairing by the ILO and IARC.	
ILO guidance notes	Nasal cancer caused by nickel is listed. "There is sufficient evidence in humans for the carcinogenicity of mixtures containing nickel compounds and nickel metal, as these agents can cause cancers of the lung, nasal cavity, and paranasal sinuses. Nickel compounds of industrial relevance that have been observed to be more frequently associated with increased cancer risks include nickel oxide, nickel hydroxide, nickel subsulphide, nickel sulphate, and nickel chloride." Cancers of the nasal cavity are rare in the general population and are often associated with specific chemical exposures or occupational settings.[1]	
IARC advice	IARC states that "there is sufficient evidence in humans for the carcinogenicity of mixtures that include nickel compounds and nickel metal. These agents cause cancers of the lung and of the nasal cavity and paranasal sinuses."[7]	
NIOSH advice	NIOSH notes that nickel is a potential occupational carcinogen. It lists nasal cavities (as well as lungs) as the target organs of relevance. Exposure routes are inhalation, skin and/or eye contact.[10]	
Deemed Diseases List advice	Cancer of the nasal cavity and para-nasal sinuses caused by nickel is listed.[4]	
Existing Schedule 2 entry	Lung cancer caused by nickel is listed.	
Summary of Independent Panel's assessment		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on clinical experience, there is a strong association between occupational nickel exposure and nasal cancer. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases*[1] report and IARC *Monographs Vol 100C.*[7]

Evidence for the Independent Panel's review		
	Consistency or reproducibility	Based on clinical experience, there is a consistent association between occupational nickel exposure and nasal cancer. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases*[1] report and IARC *Monographs Vol 100C.*[7]
	Specificity	The relationship between nickel and nasal cancer is well defined.
	Temporality or time sequence	Nasal cancer occurs after nickel exposure. Minimum exposure duration is six months, with no maximum latency period stated.[1]
	Biological gradient	Yes. There is a dose-response relationship between nickel and nasal cancer.[1,7]
	Biological plausibility	Yes. It is biologically plausible that nickel exposure can cause nasal cancer.[1,7]
	Coherence	Synthesis of evidence presented by the ILO and IARC concludes that there is a cause-effect relationship between nickel exposure and nasal cancer.[1]
	Analogy	Schedule 2 accepts that nickel inhalation causes lung cancer. ILO and IARC states that the same exposure type and route can also cause nasal cancer.
	Experimental evidence (if relevant)	Not relevant for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on clinical experience and supported by the evidence presented by the ILO and IARC, there is sufficiently strong causal evidence linking nickel exposure and nasal cancer.
	Proportion of work cases	Accurate exposure data for nickel and nasal cancer is not available for Aotearoa New Zealand at this time.
Independent Panel recommendation	**Recommend inclusion on Schedule 2 as there is a well-established and accepted relationship. No further evidence review required.**	
Suggested wording to incorporate into Schedule 2	New entry: Nasal cancer diagnosed caused by occupational exposure to nickel fumes, dusts, or mists.	

2.1.5 Potroom emissions and asthma

Evidence for the Independent Panel's review		
Exposure	Potroom emissions (including fluorine and aluminium)	
Related diseases	Asthma	
Summary statement	Sufficient causal relationship based on clinical experience of the Independent Panel, supported by designation as an occupational exposure/disease pairing by the ILO.	
ILO guidance notes	Potroom asthma caused by fluorine and aluminium is listed. "Occupational exposure occurs in people employed in the industrial preparation of fluorinated chemicals. The term potroom arises from the use of metal pots for the preparation of aluminium by electrolysis of a high-temperature molten mixture of alumina (purified bauxite), cryolite and sodium fluoride. This process is accompanied by emissions of dust and gases, which are able to cause an asthma-like syndrome known as potroom asthma, a very relevant health issue among potroom workers, smelters and casters. The most likely causative agents are irritant airborne particulates and fumes containing gaseous hydrogen fluoride, cryolite, and other elements that may be adsorbed onto aluminium. Elicitation of the disease can be observed for low dose exposures."[1]	
IARC advice	Not relevant for this disease (not cancer).	
NIOSH advice	Exposure routes include inhalation. Associated symptoms include respiratory irritation laryngeal spasm, wheezing and pulmonary edema.[11]	
Deemed Diseases List advice	Fluorine is included as an acute poisoning exposure and is linked to manufacturing. Neither aluminium or potroom asthma are listed.[4]	
Existing Schedule 2 entry	Occupational asthma caused by sensitising agents is listed.	
Summary of Independent Panel's assessment		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on clinical experience, there is a strong association between occupational potroom exposure (emissions) and asthma. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases* report.[1]
	Consistency or reproducibility	Based on clinical experience, there is a consistent association between occupational potroom exposure (emissions) and asthma. This is further supported by the ILO's *Diagnostic and exposure criteria for occupational diseases* report.[1]

Evidence for the Independent Panel's review		
	Specificity	The relationship between potroom emissions and asthma is well defined.
	Temporality or time sequence	Asthma occurs after potroom exposure to emissions. The minimum exposure duration is a few weeks and maximum latency period is three years.[1]
	Biological gradient – about dose response relationship	Yes. There is a dose-response relationship between potroom emissions and asthma.[1]
	Biological plausibility	Yes. It is biologically plausible that potroom emissions can cause asthma.[1]
	Coherence	Synthesis of evidence presented by the ILO concludes that there is a cause-effect relationship between potroom emissions and asthma.[1]
	Analogy	Many chemical exposures are known triggers of occupational asthma advised by the Independent Panel, ILO, and as acknowledged in entry 37 of Schedule 2.
	Experimental evidence	Not relevant for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on clinical experience, and supported by the evidence presented by the ILO, there is sufficiently strong causal evidence linking occupational potroom exposure (emissions) and asthma. The Panel notes that occupations are a broader exposure categorisation than what is currently listed on Schedule 2, however, the evidence highlights that is not possible to distinguish individual elements agents that might be causal.
	Proportion of work cases	Accurate exposure data for potroom emissions and asthma is not available for Aotearoa New Zealand at this time.
Independent Panel recommendation	**Recommend inclusion on Schedule 2 as there is a well-established and accepted relationship. No further evidence review required.**	
Suggested wording to incorporate into Schedule 2	Add to item 37 – "Occupational asthma caused by potroom emissions including but not limited to fluorine and aluminium, and sensitising agents inherent in the work process such as, but not limited to, isocyanates, certain wood dusts, flour dusts, animal proteins, enzymes, and latex."	

2.1.6 Welding and ocular melanoma

Evidence for the Independent Panel's review		
Exposure	Welding	
Related diseases	Ocular melanoma	
Summary statement	Sufficient causal relationship based on clinical experience of the Independent Panel, supported by designation as an occupational exposure/disease pairing by IARC.	
ILO guidance notes	Ocular melanoma caused by welding (or any other exposure) is not included in the ILO advice.	
IARC advice	"There is sufficient evidence in humans for the carcinogenicity of welding. Current evidence establishes a causal association for ocular melanoma although it is not possible without a full review of welding to attribute the occurrence of ocular melanoma to UV radiation specifically."[12]	
NIOSH advice	No advice regarding ocular melanoma available.	
Deemed Diseases List advice	Ocular melanoma caused by welding is listed.	
Existing Schedule 2 entry	No relevant existing entry.	
Summary of Independent Panel's assessment		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on clinical experience, there is a strong association between occupational welding and ocular melanoma. This is further supported by IARC *Monographs Vol 100D.*[12]
	Consistency or reproducibility	Based on clinical experience, there is a consistent association between occupational welding and ocular melanoma. This is further supported by IARC *Monographs Vol 100D.*[12]
	Specificity	The relationship between welding and ocular melanoma is well defined.
	Temporality or time sequence	Ocular melanoma occurs after welding exposure. Exposure duration and latency period are not provided by IARC.[12]
	Biological gradient	Yes. There is a dose-response relationship between welding and ocular melanoma.[12]

Evidence for the Independent Panel's review		
	Biological plausibility	Yes. It is plausible that welding can cause ocular melanoma.[12]
	Coherence	Synthesis of evidence presented by IARC notes there is sufficient evidence of the carcinogenicity of welding, including for ocular melanoma.[12]
	Analogy	Not applicable for this exposure/disease pairing.
	Experimental evidence	Not relevant for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on clinical experience, and supported by the evidence presented by IARC, there is sufficiently strong causal evidence linking occupational welding and ocular melanoma. The Panel notes that occupations are a broader exposure categorisation than what is currently listed on Schedule 2, however, the evidence highlights that is not possible to distinguish individual elements agents that might be causal.
	Proportion of work cases	Accurate exposure data for ocular melanoma and welding is not available for Aotearoa New Zealand at this time.
Independent Panel recommendation	**Recommend inclusion on Schedule 2 as there is a well-established and accepted relationship. No further evidence review required.**	
Suggested wording to incorporate into Schedule 2	Ocular melanoma diagnosed caused by occupational welding.	

2.2 Exposure/disease pairings recommended for addition to Schedule 2 with academic evidence reviews

The following exposure/disease pairings were discussed by the Independent Panel at its first meeting. At its first meeting, the independent Panel requested additional evidence to support its deliberations. At the second meeting, the independent Panel recommended that the following exposure/disease pairings be included on Schedule 2. These exposure/disease pairings have a known and well documented causational link. Included in this section are:

- 1,2 Dichloropropane and cholangiocarcinoma
- Asbestos and laryngeal cancer
- Asbestos and ovarian cancer
- Butadiene and leukaemia
- Firefighting and bladder cancer
- Firefighting and mesothelioma
- Trichloroethylene and kidney cancer
- Vinyl chloride and hepatocellular carcinoma
- Provision for future pandemic coverage

2.2.1 1,2 dichloropropane and cholangiocarcinoma

Evidence for the Independent Panel's review				
Exposure	1,2-dichloropropane (also known as propylene dichloride) (liquid)			
Related diseases	Cholangiocarcinoma (CCA) also known as bile duct cancer			
Summary statement	Sufficient causal evidence			
ILO guidance notes	1,2-dichloropropane and CCA were not linked by the ILO.			
IARC advice	"There is sufficient evidence in humans for the carcinogenicity of 1,2-dichloropropane. 1,2-dichloropropane causes cancer of the biliary tract (confirmed as cholangiocarcinoma)."[13]			
NIOSH advice	Exposure routes include inhalation, skin absorption, ingestion, skin and/or eye contact. NIOSH classifies 1,2-dichloropropane as a potential occupational carcinogen.[14]			
Deemed Diseases List advice	CCA (bile duct cancer) caused by 1,2-dichloropropane is listed.[4]			
Existing Schedule 2 entry	No relevant entry			
Evidence from academic literature	Summary of evidence search: one systematic review met the inclusion criteria (see *section 1.2.5*).			
	Study details	**Population and methods**	**Relevant data points**	**Notes**
	One narrative systematic review reported on CCA (bile duct cancer) caused by 1,2-dichloropropane.			

	Seeherunwong, A., et al. (2022)[15] **Study type:** Systematic review of 10 studies: 3 case-control, 6 cohort, 1 cross-sectional, without meta-analysis. Of these, 2 Japanese retrospective cohort studies assessed CCA and 1,2 dichloropropane (1,2 DCP) and dichloromethane (DCM). **Comparator:** Cases of CCA in occupational settings including printing (relevant for 1,2 DCP) **Countries:** Japan, Finland, Norway, Sweden, Iceland, Italy, Denmark, France, Germany, Spain.	Pooled population from two relevant studies Printing workers total: 157 Cases of CCA: 28 Ethnicity was not specifically cited but both relevant studies were conducted in Japan. Gender was calculated for Kumangi 2016 but n for each gender was not provided. Study method: Papers published between 1980 and 2020. Databases searched included PubMed, Science Direct, CINAHL, ProQuest Medical Library, Springer, Wiley online library, and the Cochrane library. The review focused on CCA, intrahepatic CCA (as distinct from other types of liver cancer), and extrahepatic CCA	Kumangi et al 2016. CCA risk in people working in printing, exposed to 1,2 DCP and DCM. Total CCA risk all workers SIR: 1.171 (95% CI: 0.682, 1.875) *NB null included in the CI* Male SIR: 1.203 (95% CI: 0.701, 1.927) *NB null included in the CI* Female SIR: <0.001 (95% CI:0, 9.426) *NB null included in the CI, p value only given here.* 1,2 DCP exposed workers SIR: 1.019 (95% CI: 0.374, 2.218) *NB null included in the CI* 1,2 DCP and DCM exposed workers SIR: 1.275 (95% CI: 0.636, 2.280) *NB null included in the CI* Cumulative 1,2 DCP exposure, no lag time Middle exposure RR: 14.9 (95% CI: 4.1, 54.3) *NB very wide CI* High exposure RR: 17.1 (95% CI: 3.8, 76.2) *NB very wide CI* p=<.001 Cumulative 1,2 DCP exposure, 5-year lag	The study authors conclude that there is a statistically significant link between 1,2-dichloropropane and CCA but all datasets provided include the in the CI. They have not provided any other data to support this statement. The study authors note this finding supports IARC's classification. Cases of CCA had a higher incidence among printers exposed to 1,2 DCP. NB: Only two small Japanese studies were used to support this analysis, both published by the same author. This study also assessed links to asbestos, shift work and endocrine disrupting compounds, all of which found a statistically significant link to cases of CCA.

Evidence for the Independent Panel's review				
		(not including the gallbladder).	Middle exposure RR: 11.4 (95% CI: 3.3, 39.6) *NB very wide CI* High exposure RR: 32.4 (95% CI: 6.4, 163.9) *NB extremely wide CI* p=<.001 <u>Kumangi et al 2013.</u> CCA risk in men working in printing, exposed to 1,2 DCP and DCM. <u>All workers:</u> SMR: 2.9 (95% CI: 1.1, 6.2) <u>Proof-printing</u> SMR: 5.0 (95% CI: 1.6, 12)	

Summary of Independent Panel's assessment		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on the evidence presented, the Independent Panel agree that there is a strong association between 1,2-dichloropropane and CCA.
	Consistency or reproducibility	Based on the evidence presented, the Independent Panel agree that the association between 1,2-dichloropropane and CCA has been consistently reproduced.
	Specificity	The relationship between 1,2-dichloropropane and CCA is well defined.
	Temporality or time sequence	CCA occurs after exposure to 1,2-dichloropropane.[13]
	Biological gradient	Yes, there is a dose-response relationship between1,2-dichloropropane and CCA.[13]
	Biological plausibility	Yes, it is plausible that 1,2-dichloropropane can cause CCA.[13]

Evidence for the Independent Panel's review		
	Coherence	Synthesis of evidence presented by IARC, as well as the systematic review summarised above, conclude there is sufficient evidence of the causal connection between 1,2-dichloropropane and CCA.[13,15]
	Analogy	Not applicable for this exposure/disease pairing.
	Experimental evidence (if relevant)	Not applicable for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on the evidence presented, the Independent Panel agree that there is a sufficiently strong causal connection between 1,2-dichloropropane and CCA.
	Proportion of work cases	ACC does not have current data about the proportion of work-related CCA claims with a link to 1,2-dichloropropane. No independent exposure data for Aotearoa New Zealand was found in the published peer-reviewed literature.
Independent Panel recommendation	**Recommend inclusion on Schedule 2**	
Suggested wording to incorporate into Schedule 2	New entry: CCA diagnosed caused by occupational exposure to 1,2-dichloropropane.	

2.2.2 Asbestos and laryngeal cancer

Evidence for the Independent Panel's review				
Exposure	Asbestos			
Related diseases	Laryngeal cancer			
Summary statement	Sufficient causal evidence			
ILO guidance notes	Laryngeal cancer caused by asbestos exposure is listed. "Laryngeal cancer has been studied in several cohort and case-control studies, conducted among populations occupationally exposed to asbestos (eg, insulation workers, asbestos miners and millers, workers in an asbestos-cement industry) in Europe, North and South America, and Asia. These investigations consistently showed a significantly positive association between asbestos exposure and cancer of the larynx."[1]			
IARC advice	"Asbestos causes mesothelioma and cancer of the lung, larynx, and ovary."[7]			
NIOSH advice	NIOSH note that asbestos exposure is associated with lung cancer and mesothelioma, but do not mention laryngeal cancer.[16]			
Deemed Diseases List advice	Laryngeal cancer caused by asbestos is listed.			
Existing Schedule 2 entry	Only lung cancer and mesothelioma caused by asbestos are listed.			
Evidence from academic literature	Summary of evidence search: one meta-analysis met the inclusion criteria (see *section 1.2.5*). Since IARC's publication in 2009, studies testing the association between laryngeal cancer and asbestos were not identified. The IOM meta-analysis from 2006 which was one of the key studies IARC referenced in 2009, is presented here.			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

	Institute of Medicine (2006)[17] **Study type:** Meta-analysis of 35 cohort studies and 18 case-control studies that examined diagnosis or death from laryngeal cancer among people with any occupational exposure to asbestos compared with people in the general population. **Comparator**: Cases/deaths of laryngeal cancer connected to exposure to asbestos compared to the general population. **Countries:** North America, South America, Europe, and Japan.	Population: Not provided Data on ethnicity or gender not provided. Methods: Databases searched included Medline and Embase Statistical modelling included Poisson regression (cohort studies) and DerSimonian and Laird random-effects model (case-control).	The pooled RR of laryngeal cancer among persons with any occupational exposure to asbestos compared with those who reported no exposure: Cohort: 1.40 (95% CI: 1.19, 1.64) Case-control: 1.43 (95% CI: 1.15, 1.78) Breakdown (where data was available) Cohort studies RR: 1.40 (95% CI: 1.19, 1.64) Study population: 35 2.02 (95% CI: 1.64, 2.47) Study population: 11 2.57 (95% CI: 1.47, 4.49) Study population: 11 Case-control studies RR: 1.43 (95% CI: 1.15, 1.78) Study population: 15 1.21 (95% CI: 1.04, 1.40) Study population: 10 2.56 (95% CI: 1.20, 5.43) Study population: 5 1.18 (95% CI: 1.01, 1.37) Study population: 7 1.58 (95% CI: 0.86, 2.91) Study population: 3 1.38 (95% CI: 1.02,1.86) Study population: 7	IOM concluded that the evidence is sufficient to infer a causal relationship between asbestos exposure and laryngeal cancer. "The larger cohort studies consistently show increased risk of laryngeal cancer in asbestos-exposed workers employed in a wide array of industries and in a large cohort of workers with asbestosis. There is some evidence of a dose-response relationship in the meta-analyses."[17]

Evidence for the Independent Panel's review				
			1.53 (95% CI: 1.21, 1.93) Study population: 7	
Summary of Independent Panel's assessment				
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**		
	Strength of association	Based on the evidence presented, the Independent Panel agree that there is a strong association between asbestos and laryngeal cancer.		
	Consistency or reproducibility	Based on the evidence presented, the Independent Panel agree that the association between asbestos and laryngeal cancer has been consistently reproduced.		
	Specificity	The relationship between asbestos and laryngeal cancer is well defined.		
	Temporality or time sequence	Laryngeal cancer occurs after exposure to asbestos.[7]		
	Biological gradient	Yes, there is a dose-response relationship between asbestos and laryngeal cancer.[7]		
	Biological plausibility	Yes, it is plausible that asbestos can cause laryngeal cancer.[7]		
	Coherence	Synthesis of evidence presented by IARC and IOM conclude there is sufficient evidence of the causal connection between asbestos and laryngeal cancer.[7,17]		
	Analogy	Not applicable for this exposure/disease pairing.		
	Experimental evidence (if relevant)	Not applicable for this exposure/disease pairing.		
	Sufficiently strong causal evidence	Based on the evidence presented, the Independent Panel agree that there is a sufficiently strong causal connection between asbestos and laryngeal cancer.		
	Proportion of work cases	ACC does not have current data about the proportion of work-related laryngeal cancer claims with a link to asbestos exposure. No independent exposure data for Aotearoa New Zealand was found in the published peer-reviewed literature.		

Evidence for the Independent Panel's review	
Independent Panel recommendation	**Recommend inclusion on Schedule 2**
Suggested wording to incorporate into Schedule 2	Add to entry 2: "Lung cancer, mesothelioma, ovarian cancer, and laryngeal cancer diagnosed caused by occupational exposure to asbestos"

2.2.3 Asbestos and ovarian cancer

Evidence for the Independent Panel's review				
Exposure	Asbestos			
Related diseases	Ovarian cancer			
Summary statement	Sufficient causal evidence			
ILO guidance notes	Ovarian cancer caused by asbestos is listed. "Investigations conducted on occupationally exposed female workers (e.g., employed in factories manufacturing asbestos-containing gas masks or asbestos-board insulation, and in asbestos-textile or asbestos-cement plants) showed positive associations with ovarian cancer, further supported by evidence arising among environmentally exposed females. Data are still insufficient to document specific histopathological types of ovarian cancers caused by asbestos exposure."[1]			
IARC advice	IARC reports asbestos to have a 'clearly established' causal association with ovarian cancer, based primarily on five cohort studies. "Asbestos causes mesothelioma and cancer of the lung, larynx, and ovary."[7]			
NIOSH advice	NIOSH notes the link between asbestos and mesothelioma and lung cancer but does not mention ovarian cancer.[16]			
Deemed Diseases List advice	Ovarian cancer caused by asbestos is listed.			
Existing Schedule 2 entry	Lung cancer and mesothelioma caused by asbestos are listed.			
Evidence from academic literature	Summary of evidence search: a total of three returns met the inclusion criteria (see *section 1.2.5*). Two meta-analyses and one literature review are summarised below. Earlier case control and cohort studies about ovarian cancer and asbestos exposure are captured in the meta-analyses.			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

	Camargo, M. C, et al. (2011)[18] **Study type:** Meta-analysis of 18 cohort studies **Comparator**: SMRs (n=17) or SIRs (n=1) of women occupationally exposed to asbestos, compared with the expected incidence or mortality from the general population. **Countries:** United States, United Kingdom, Germany, Italy, Poland, Australia, France	Pooled population: 125 deaths from and 1 incidence of ovarian cancer. Ovarian cancer cases from women, though studies also assessed other cancers including lung cancer – further details not provided. Ethnicity not assessed. Study method: Papers published before 2001. Only papers that included an estimate of risk (i.e., SMR or SIR) and where there was evidence of occupational exposure to asbestos were included. Further information on quality assessment not specified. Overall pooled SMR estimates and their	Overall pooled SMR estimate for ovarian cancer with occupational asbestos exposure: 1.77 (95% CI: 1.37, 2.28), with a moderate degree of heterogeneity among the studies (I^2 = 35.3%, p=.061). Individual SMRs or SIRs of cohort studies. One of the below is an SIR and the rest are SMRs though the authors do not specify which is the SIR. ***Studies where CIs do not include the null*** Acheson et al. (1982) 2.75 (95% CI: 1.42, 4.81) Ovarian cancer cases: 12 Cohort size: 757 Germani et al. (1999) 5.26 (95% CI: 1.43, 13.47) *NB: wide CI* Ovarian cancer cases: 4 Cohort size: 276 Berry et al. (2000) 2.53 (95% CI: 1.16, 4.80) *NB: wide CI* Ovarian cancer cases: 9 Cohort size: 700 Pira et al. (2007) 2.83 (95% CI: 1.22, 5.57) Ovarian cancer cases: 8 Cohort size: 1,077	The study authors acknowledge their findings support IARC's conclusion that exposure to asbestos is associated with increased risk of ovarian cancer; however, some studies cited have the null in the CI, reducing statistical significance. The study authors have not provided any other data to support their conclusion. There were stronger effects observed for European cohorts that cohorts from other geographic locations. The study authors note that samples size reduced heterogeneity – the smaller the cohort size, the larger the SMR was related to limited cohort size (<500) in the three studies of women compensated for asbestosis. Sample size was no longer an important predictor once the studies of women with asbestosis and gas mask production were removed from the analysis. "Based on the sensitivity analysis in this study, it

		corresponding 95% CIs were obtained using random-effects methods. Databases searched included PubMed (Medline).	Magnani et al. (2008) 2.27 (95% CI: 1.04, 4.32) Ovarian cancer cases: 9 Cohort size: 777 ***Studies where CIs include the null*** Gardner et al. (1986) 1.11 (95% CI: 0.23, 3.25) Ovarian cancer cases: 5 Cohort size: 657 Newhouse and Sullivan (1989) 1.08 (95% CI: 0.61, 1.79) Ovarian cancer cases: 11 Cohort size: 4,345 Rösler et al. (1994) 1.09 (95% CI: 0.13, 3.95) Ovarian cancer cases: 2 Cohort size: 616 Tarchi et al. (1994) 4.76 (95% CI: 0.58, 17.2) *NB: wide CI* Ovarian cancer cases: 2 Cohort size: 616 Szeszenia-Dabrowska et al. 2002 0.79 (95% CI: 0.02, 4.39) Ovarian cancer cases: 1 Cohort size: 490 Mamo (2004) 1.28 (95% CI: 0.02, 7.12)	appears unlikely that the results can be fully explained by misclassification of ovarian cancer and peritoneal mesothelioma or other sources of bias and confounding."[18]

			NB: wide CI Ovarian cancer cases: 1 Cohort size: 645 Wilczyn´ska et al. (2005) 1.76 (95% CI: 0.76, 3.47) Ovarian cancer cases: 8 Cohort size: 1,201 McDonald et al. (2006) 1.80 (95% CI: 0.9, 3.3) Ovarian cancer cases: 10 Cohort size: 1,073 Hein et al. (2007) 0.62 (95% CI: 0.23, 1.35) Ovarian cancer cases: 6 Cohort size: 1,265 Loomis et al. (2009) 1.23 (95% CI: 0.56, 2.33) Ovarian cancer cases: 9 Cohort size: 1,795 Reid et al. (2009) 0.65 (95% CI: 0.02, 3.64) Ovarian cancer cases: 1 Cohort size: 416 Harding et al. (2009) 1.12 (95% CI: 0.66, 1.80) Ovarian cancer cases: 17 Cohort size: 4,495 Clin et al. (2009) 1.60 (95% CI: 0.33, 4.67)	

Evidence for the Independent Panel's review				
			Ovarian cancer cases: 3 Cohort size: 420	
	Reid, A., et al. (2011)[19] **Study type:** Meta-analysis of 14 cohort and 2 case-control studies. **Comparator**: Ovarian cancer cases in asbestos exposed population compared with expected number of cases from general population. **Countries:** United Kingdom, Germany, Italy, Poland, United States, Norway, Finland.	<u>Pooled population:</u> 906,579 women exposed to asbestos and 5,240 ovarian cancer cases. Ethnicity not assessed. <u>Methods:</u> Papers published between 1950 to December 2008. Databases searched were Medline. Modelling included fixed effects and random effects There is some overlap with Camargo et al. (above) but also a number of different studies selected between the two meta-analyses.	Pooled SMR of women occupationally exposed to asbestos with ovarian cancer incidence or mortality (n=16): 1.75 (95% CI: 1.45, 2.10) Cohort-studies only (n=14): 1.75 (95% CI: 1.45, 2.12) Case control studies only (n=2): 1.69 (95% CI: 0.76, 3.73) *NB: CI includes the null* Cohort studies that reviewed ovarian pathology (n=5): 1.53 (95% CI: 1.2, 1.95)	The study authors conclude that the meta-analysis supports IARC's classification of asbestos causing ovarian cancer but remain concerned about the quality of the data from the original studies (a small number of ovarian cases reported in the cohort and case control studies and potentially inaccurate outcome data).

Evidence for the Independent Panel's review				
	Slomovitz, B., et al. (2021)[20] **Study type:** Literature review **Comparator:** Asbestos and ovarian cancer **Country:** United States	Population 3,935 women exposed to asbestos. Method Reviewing previously published evidence on the association between asbestos and ovarian cancer. It cites the five cohort studies that IARC cited as the basis for its 2009 classification of asbestos as a cause of ovarian cancer. Studies referenced we published between 1982 - 2008 Some overlap of cited studies with above meta-analyses.	Acheson et al. (1982) cohort study SMR: 2.75 (95% CI: 1.42, 4.81) *757 women exposed to crocodolite fibres* SMR: 1.48 (95% CI: 0.48, 3.44) *570 exposed to chrysotile* Wignall and Fox. (1982) cohort study SMR: 2.13, p<.01 500 women with crocodolite exposure Berry et al. (2000) cohort study SMR: 2.53 (95% CI: 1.16, 4.80) 700 women exposed to multiple fibre types Germani et al. (1999) cohort study SMR: 4.77 (95% CI: 2.1, 9.06) 631 women from registry of women exposed to any fibre type of asbestos Magnani et al. (2008) cohort study SMR: 2.27, p<.05 777 women exposed to mixed fibres	IARC found asbestos to have a 'clearly established' causal association with ovarian cancer, based primarily on five cohort studies. This study notes that without pathological data, it is impossible to determine differences in types of ovarian cancer caused by asbestos.[20]
Summary of Independent Panel's assessment				
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**		

Evidence for the Independent Panel's review		
	Strength of association	Based on the evidence presented, the Independent Panel agree that there is a strong association between asbestos and ovarian cancer.
	Consistency or reproducibility	Based on the evidence presented, the Independent Panel agree that the association between asbestos and ovarian cancer has been consistently reproduced.
	Specificity	The relationship between asbestos and ovarian cancer is well defined.
	Temporality or time sequence	Ovarian cancer occurs after exposure to asbestos.[7]
	Biological gradient	Yes, there is a dose-response relationship between asbestos and ovarian cancer.[7]
	Biological plausibility	Yes, it is plausible that asbestos can cause ovarian cancer.[7]
	Coherence	Synthesis of evidence presented by IARC, as well as the evidence summarised above, conclude there is sufficient evidence of the causal connection between asbestos and ovarian cancer.[7,18–20]
	Analogy	Not applicable for this exposure/disease pairing.
	Experimental evidence (if relevant)	Not applicable for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on the evidence presented, the Independent Panel agree that there is a sufficiently strong causal connection between asbestos and ovarian cancer.
	Proportion of work cases	ACC does not have current data about the proportion of work-related ovarian cancer claims with a link to asbestos exposure. No independent exposure data for Aotearoa New Zealand was found in the published peer-reviewed literature.
Independent Panel recommendation	**Recommend inclusion on Schedule 2**	
Suggested wording to incorporate into Schedule 2	Add to entry 2: "Lung cancer, mesothelioma, ovarian cancer, and laryngeal cancer diagnosed caused by occupational exposure to asbestos"	

2.2.4 Butadiene and leukaemia

Evidence for the Independent Panel's review				
Exposure	Butadiene			
Related diseases	Leukaemia			
Summary statement	Sufficient causal evidence			
ILO guidance notes	Butadiene is not listed a relevant exposure for leukaemia by the ILO.			
IARC advice	"There is sufficient evidence in humans for the carcinogenicity of 1,3-butadiene in humans (group 1)."[21] Individual cancers are not specified by IARC in its designation, but leukaemia (as well as lymphoma) are noted as the relevant cancers in the epidemiological studies cited by IARC in their assessment of butadiene carcinogenicity.			
NIOSH advice	Epidemiological studies of workers employed in facilities producing styrene-butadiene rubber indicated an increased, but not statistically significant, risk of mortality from neoplasms of the lymphatic and hematopoietic tissues and from leukaemia. Based on these data, NIOSH recommends that 1,3-butadiene be regarded as a potential occupational carcinogen and teratogen and as a possible reproductive hazard.[22]			
OSHA advice	"Several human epidemiological studies have shown an increase in cardiovascular diseases and cancer; however, due to the small numbers of cancers and confounding factors such as smoking, and simultaneous exposure to benzene and styrene, a true causal relationship cannot be established. Experiments involving chronic exposures to mice and rats have shown a strong causal relationship between 1,3-butadiene exposure and cancer. Animal studies have also shown reproductive and developmental problems. Based on human and animal studies, the Environmental Protection Agency has classified 1,3-butadiene as a known human carcinogen. The American Conference of Governmental Industrial Hygienists has given 1,3-butadiene a rating of A2, suspected human carcinogen."[23]			
Deemed Diseases List advice	Leukaemia caused by butadiene is listed as an entry on the Deemed Diseases List.			
Existing Schedule 2 entry	No relevant entry.			
Evidence from academic literature	Summary of evidence search: one cohort study met the inclusion criteria (see *section 1.2.5*).			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

Evidence for the Independent Panel's review				
	Sathiakumar, N., et al. (2021)[24] Study type: Cohort study Comparator: Synthetic rubber polymer workers with exposure to butadiene (and styrene) and cases of leukaemia compared to workers who were not exposed to butadiene or styrene. Countries: United States and Canada	Population: 21,087 workers across 8 polymer plants: 14,004 of whom were exposed to butadiene and 136 deaths from leukaemia. Men: 16,579 Women: 4,508 Black: 2,413 White: 18,674 No other ethnic groups reported. Methods: Longitudinal cohort study (1943 to 2009) Exposure: butadiene or styrene measured in parts per million-years (ppm-years) Outcome: all leukaemia, lymphoid leukaemia, myeloid leukaemia, acute myeloid leukaemia, NHL, multiple myeloma and all B-cell malignancies.	Adjusted RR for butadiene and leukaemia (95% CI) for quartiles of increasing levels of exposure: Q1 (<34 ppm-years) 1.04 (95%CI: 0.6, 1.83) Q2 (34 ppm-years) 1.37 (95% CI: 0.76, 2.46) Q3 (121.28 ppm-years) 1.60 (95% CI: 0.87, 2.94) Q4 (363.64 ppm-years) 2.53 (95% CI: 1.37, 4.67) Exposure–response trend was statistically significant for all leukaemia (p=.014)	This study confirms a connection between butadiene and leukaemia, with a co-exposure to styrene, supporting IARC's classification of butadiene as a known human carcinogen. Results supported an association between butadiene and lymphoid leukaemia, but not myeloid leukaemia.
Summary of Independent Panel's assessment				
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**		
	Strength of association	Based on the evidence presented, the Independent Panel agree that there is a strong association between butadiene and leukaemia.		
	Consistency or reproducibility	Based on the evidence presented, the Independent Panel agree that the association between butadiene and leukaemia has been consistently reproduced.		

Evidence for the Independent Panel's review		
	Specificity	The relationship between butadiene and leukaemia is well defined.
	Temporality or time sequence	Leukaemia occurs after exposure to butadiene.[21]
	Biological gradient	Yes, there is a dose-response relationship between butadiene and leukaemia.[21]
	Biological plausibility	Yes, it is plausible that butadiene can cause leukaemia.[21]
	Coherence	Synthesis of evidence presented by IARC, as well as the cohort study summarised above, conclude there is sufficient evidence of the causal connection between butadiene can cause leukaemia.[21,24]
	Analogy	Not applicable for this exposure/disease pairing.
	Experimental evidence (if relevant)	Not applicable for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on the evidence presented, the Independent Panel agree that there is a sufficiently strong causal connection between butadiene and leukaemia.
	Proportion of work cases	ACC does not have current data about the proportion of work-related leukaemia cases connected with butadiene exposure. No independent exposure data for Aotearoa New Zealand was found in the published peer-reviewed literature.
Independent Panel recommendation	**Recommend inclusion on Schedule 2**	
Suggested wording to incorporate into Schedule 2	New Entry: Leukaemia diagnosed caused by butadiene exposure.	

2.2.5 Firefighting and bladder cancer

Evidence for the Independent Panel's review				
Exposure	Firefighting			
Related diseases	Bladder cancer			
Summary statement	Sufficient causal evidence			
ILO guidance notes	Firefighting not specifically listed as an exposure.			
IARC advice	IARC states that there is a causational relationship between firefighting and bladder cancer. "Occupational exposure as a firefighter was classified as "carcinogenic to humans" (Group 1) based on "sufficient" evidence for cancer in humans. The Working Group concluded that there was "sufficient" evidence in humans for mesothelioma and bladder cancer. The Group 1 evaluation for occupational exposure as a firefighter should be presumed to apply to all firefighters (including volunteers) and to both men and women. Occupational exposure as a firefighter is complex and includes a variety of hazards resulting from fires and non-fire events. Firefighters can have diverse roles, responsibilities, and employment (eg, full-time, parttime, or volunteer) that vary widely across countries and change over their career. In the Working Group's meta-analysis of ten studies [for bladder cancer], the increased risk estimate was small in magnitude (16 percent) but was statistically precise and had low heterogeneity (95% CI: 8, 26 percent, I^2=0)"[25] Chemicals of note: Polycyclic aromatic hydrocarbons (PAHs), asbestos, PFAS, flame retardants, smoke, and diesel exhaust.			
NIOSH advice	NIOSH acknowledge that firefighters are at higher risk of certain types of cancers, and link to the IARC publication referenced above.[26]			
Deemed Diseases List advice	Bladder cancer caused by 2-naphthylamine, benzidine, cyclophosphamide, ionizing radiation, ortho-toluidine, PAHs is included.			
Existing Schedule 2 entry	Bladder cancer caused by 2-naphthylamine, benzidine, 4-aminobiphenyl, N, N-Bis (2-chloroethyl)-2-naphthylamine, other aromatic amines, or poly-cyclic aromatic hydrocarbons is listed.			
Evidence from academic literature	Summary of evidence search: a total of four returns met the inclusion criteria (see *section 1.2.5*). Three systematic reviews with meta-analysis and one systematic review (without meta-analysis) are summarised below.			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

Evidence for the Independent Panel's review				
	Casjens et al. (2020)[27] **Study type:** Systematic review and meta-analysis of 25 cohort cases assessing cancer in firefighters – 14 of which were relevant to bladder cancer. **Comparator:** Cancer incidence in firefighters over time and in different geographic areas. **Countries:** United States, Canada. Korea, France, New Zealand, Australia, Sweden NB: The one New Zealand study included assessed testicular cancer rates in firefighters.	<u>Population:</u> Population breakdowns not provided by cancer. 248,044 participants across all studies in meta-analysis. Data on ethnicity and gender not provided. <u>Methods:</u> Database searched was PubMed. Search dates were up to December 2018. Model used was inverse-variance random-effect meta-analyses. Meta-relative risk estimates (mSIRs, mSMRs) and 95% CI were assessed.	Meta-relative risk estimates for overall bladder cancer <u>incidence</u>: mSIR: 1.14 (95% CI: 1.04, 1.23) Statistically significant incidence of blader cancer in firefighters. Meta-relative risk estimates for bladder cancer <u>mortality mSMR</u>: 1.44 (95% CI: 0.82, 2.06)	Statistically significant elevated incidence and mortality ratio estimates were observed for bladder cancer in firefighters. The CI includes the null so this output should be interpreted with caution. The study authors have not provided any other data to support this statement. "The objective of this study was to conduct a systematic review and meta-analysis to evaluate the cancer risks among firefighters in the time course and from different geographical areas." 26 different cancer locations were considered, including (1) bladder and (2) urinary tract. "Regional differences were observed for bladder cancer – incidence ratios of bladder cancer in Firefighters were statistically significant in North America, but not in Europe, Korea, or Australia and New Zealand. However only one New Zealand and one Australian study was considered in this analysis."

Evidence for the Independent Panel's review				
	Soteriades, E.S., et al. (2019)[28] **Study type:** Systematic review and meta-analysis of 49 studies – 26 cohort, 17 case control and 6 were surveillance or other study designs (for all cancers) **Comparator:** Association between firefighting and cancer compared to general populations **Countries:** United States, Canada, New Zealand, Australia, Europe NB: Data was not presented by paper, or country (only presented by cancer type) so data from New Zealand studies was not able to be extracted.	Pooled population: Not provided. Breakdown of studies by cancer type was not provided. Methods: Databases searched included EMBASE, Biosis, NIOSHTIC2, Web of Science, Cancerlit, and HealthStar, for the period between 1966 to January 2007. Studies were assessed for relevance and quality against a modified MOOSE guideline (-1, 0, +1 rating system). Inverse variance meta-analysis methodology used for pooled statistical information.	Pooled Estimates for the association of firefighting with bladder cancer Combined incidence and mortality: 1.18 (95% CI: 1.01, 1.36), p=<0.05 Statistically significant association. Incidence – 'good' studies (n=6) 1.18 (95% CI: 0.97, 1.43) Incidence – all studies (n=9) 1.06 (95% CI: 0.88 , 1.27) Mortality – 'good' studies (n=9) 1.39 (95% CI: 0.91, 2.11) Mortality – all studies (n=17) 1.28 (95% CI: 1.05, 1.56), p=.05 P value only given for mortality/all studies.	The study authors did not reach a definitive conclusion regarding causality. The pooled risk estimate for mortality and incidence of bladder cancer in firefighters produced a statistically significant result; however, some of the CIs in the breakdowns of this data included the null, so this data should be interpreted with caution. The study authors note that limitations with the original studies preclude definitive causality. These limitations include: challenges identifying associations with occupational exposure and cancer risk personal risk factors (i.e., family histories of some cancer sites) that could not be controlled for in the meta-analysis small number of observed cases in some studies and concerns regarding the control/reference groups in some individual studies. The study authors conclude that the statistical results are consistent with other quantitative estimates and the majority of previous reports. 24 cancer sites assessed, including (1) bladder and (2) urinary.

Evidence for the Independent Panel's review				
	Jalilian, H., et al. (2019)[29] **Study type:** Systematic review of 50 papers (16 case-control, 34 cohort), 48 of which were used in the meta-analysis. 24 of these papers addressed bladder cancer. **Comparator:** Cancer incidence and mortality amongst firefighters. Many types of cancers assessed. **Countries:** United States, Canada, New Zealand, Australia, Turkey, Germany, France, Netherlands, South Korea, Sweden, Denmark, United Kingdom, NB: Breakdown of studies by cancer type was not provided.	<u>Pooled population:</u> 1,182,079 (all participants – data stratified by cancer type not available) Data on ethnicity and gender not provided. <u>Methods:</u> Databases searched included PubMed, Embase, and Web of Science up to January 1, 2018. Meta-analysis was random effects. Systematic review and meta-analysis were performed in accordance with the PRISMA guidelines.	Summary incidence risk estimates for bladder cancer in firefighters: SIRE: 1.12 (95% CI: 1.04, 1.21)	The study authors conclude that incidence of bladder cancer is possibly increased among firefighters; however, data beyond a summary risk estimate was not provided in-text or in the supplementary information. The study authors did not detail limitations of their study or the datasets they used. There were a large number of cancers assessed in this meta-analysis, elevated SIREs or SMREs were also found for the following cancer sites: Colon Rectal Prostate Testis Thyroid Pleura Melanoma NHL

Evidence for the Independent Panel's review				
	Laroche, and L'Esperance (2021)[30] **Study type:** Systematic review of 11 systematic reviews, 9 of which related to bladder cancer. **Comparator:** Cancer incidence and mortality among firefighters compared to the general population. **Country:** Not provided, though likely similar to the countries listed above.	<u>Population</u> Not provided <u>Methods</u> Databases searched included MEDLINE (PubMed), Embase, Cochrane Library, Centre for Reviews and Dissemination, Web of Science, CINAHL, PsycNet, ABI/INFORM Global and SCOPUS. Search dates were from the inception of the database up to 12 October 2019. The methodological quality of the systematic reviews included were assessed using the ROBIS tool. This review was performed according to the PRISMA statement.	Incidence of bladder cancer in firefighters risk estimates sRR: 1.36 (95% CI: 1.01, 1.80) mRR: 1.12 (95% CI: 1.01, 1.26) SIRE: 1.12 (95% CI: 1.04, 1.21) Mortality of bladder cancer in firefighters risk estimates (95% CI) SMR: 1.23 (95% CI: 1.05, 1.44) sRE: 1.20 (95% CI: 0.97, 1.48) *CI includes the null* sRR: 1.07 (95% CI: 0.95, 1.15) *CI includes the null* SMRE: 1.22 (95% CI: 0.93, 1.60) *CI includes the null*	An increase of the incidence or risk of bladder cancer was consistently reported in the systematic reviews for firefighters compared to the general population. Mortality is less clear, with several of the CI data outputs including the null. The study authors note that observations from this review should be interpreted with caution as the methodological quality of the reviewed systematic reviews is generally low: in many instances inclusion and exclusion criteria for original studies are absent or not explicit, methodology poorly described, minimal information on databases searched and search strategies, and limited QA processes/ A large number of cancers assessed in this review, elevated cancer incidences in firefighters was found for: Rectal Prostate Testicular Mesothelioma Melanoma Elevated cancer mortality in firefighters was found for rectal and NHL.
Summary of Independent Panel's assessment				

Evidence for the Independent Panel's review		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on the evidence presented, the Independent Panel agree that there is a strong association between firefighting and bladder cancer.
	Consistency or reproducibility	Based on the evidence presented, the Independent Panel agree that the association between firefighting and bladder cancer has been consistently reproduced.
	Specificity	The relationship between firefighting and bladder cancer is well defined.
	Temporality or time sequence	Bladder cancer occurs after firefighting exposure.[25]
	Biological gradient	Yes, there is a dose-response relationship between firefighting and bladder cancer.[25]
	Biological plausibility	Yes, it is plausible that firefighting can cause bladder cancer.[25]
	Coherence	Synthesis of evidence presented above, concludes there is sufficient evidence of the causal connection between firefighting and bladder cancer.[25,27–30]
	Analogy	Not applicable for this exposure/disease pairing.
	Experimental evidence (if relevant)	Not applicable for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on the evidence presented, the Independent Panel agree that there is a sufficiently strong causal connection between firefighting and bladder cancer. The Panel notes that occupations are a broader exposure categorisation than what is currently listed on Schedule 2, however, the evidence highlights that is not possible to distinguish individual elements agents that might be causal.
	Proportion of work cases	ACC does not have current data about the proportion of work-related bladder cancer claims with a link to firefighting exposure. No independent exposure data for Aotearoa New Zealand was found in the published peer-reviewed literature.

Evidence for the Independent Panel's review	
Independent Panel recommendation	**Recommend inclusion on Schedule 2**
Suggested wording to incorporate into Schedule 2	Amend entry 33: **"**Bladder carcinoma diagnosed caused by 2-naphthylamine, benzidine, 4-aminobiphenyl, N, N-Bis (2-chloroethyl)-2-naphthylamine, other aromatic amines, poly-cyclic aromatic hydrocarbons, or firefighting."

2.2.6 Firefighting and mesothelioma

Evidence for the Independent Panel's review				
Exposure	Firefighting			
Related diseases	Mesothelioma			
Summary statement	Sufficient causal evidence			
ILO guidance notes	Firefighting not specifically listed as an exposure.			
IARC advice	IARC states that there is a causational relationship between firefighting and mesothelioma. "Occupational exposure as a firefighter was classified as "carcinogenic to humans" (Group 1) based on "sufficient" evidence for cancer in humans. The Working Group concluded that there was "sufficient" evidence in humans for mesothelioma and bladder cancer. The Group 1 evaluation for occupational exposure as a firefighter should be presumed to apply to all firefighters (including volunteers) and to both men and women. Occupational exposure as a firefighter is complex and includes a variety of hazards resulting from fires and non-fire events. Firefighters can have diverse roles, responsibilities, and employment (e.g., full-time, parttime, or volunteer) that vary widely across countries and change over their career. For these combined studies, the Working Group meta-analysis estimated a 58 percent higher risk (95% CI: 14–120 percent) for mesothelioma among firefighters compared with mostly general populations".[25]			
NIOSH advice	NIOSH acknowledges that firefighters are at higher risk of certain types of cancers, and link to the IARC publication referenced above.[26]			
Deemed Diseases List advice	Mesothelioma caused by asbestos is listed.			
Existing Schedule 2 entry	Mesothelioma caused by asbestos is listed.			
Evidence from academic literature	Summary of evidence search: Three articles met the inclusion criteria (see *section 1.2.5*). Two systematic reviews with meta-analysis and one systematic review (without meta-analysis) are summarised below.			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

Evidence for the Independent Panel's review				
	Casjens et al. (2020)[27] **Study type:** Systematic review and meta-analysis of 25 cohort cases – 2 of which were relevant to mesothelioma. **Comparator:** Cancer incidence in firefighters over time and in different geographic areas compared to general populations. **Countries:** United States, Canada. Korea, France, New Zealand, Australia, Sweden	Population: Population breakdowns not provided by cancer. 248,044 participants across all studies in meta-analysis. Data on ethnicity and gender not provided. Methods: Database searched was PubMed. Search dates were up to December 2018 Model used was inverse-variance random-effect meta-analyses. Meta-relative risk estimates (mSIRs, mSMRs) and 95% CI were assessed.	Meta-relative risk estimates for bladder cancer incidence: mSIR: 1.46 (95% CI: 1.01, 1.90)	The study authors highlight a statistically significant incidence of mesothelioma in firefighters. No further analysis or discussion of mesothelioma was provided. Data for cancer mortality not available for mesothelioma. It is worth noting that there are only 2 studies relevant to mesothelioma in this analysis.

Evidence for the Independent Panel's review				
	Jalilian, H., et al. (2019)[29] **Study type:** Systematic review of 50 papers (16 case-control, 34 cohort), 48 of which were used in the meta-analysis. 24 of these papers addressed bladder cancer. **Comparator:** Cancer incidence and mortality amongst firefighters. Many types of cancers assessed. **Countries:** United States, Canada, New Zealand, Australia, Turkey, Germany, France, Netherlands, South Korea, Sweden, Denmark, United Kingdom, NB: Breakdown of studies by cancer type was not provided.	Pooled population: 1,182,079 (all participants – data stratified by cancer type not available) Data on ethnicity and gender not provided. Methods: Databases searched included PubMed, Embase, and Web of Science up to 1 January 2018. Meta-analysis was random effects. Systematic review with meta-analysis was performed in accordance with the PRISMA guidelines.	Summary incidence risk estimates for mesothelioma in firefighters: SIRE: 1.60 (95% CI: 1.09, 2.34) Increased cancer incidence by 60%. Summary mortality risk estimates for mesothelioma in firefighters: SMRE: 1.33 *CI not provided.*	The findings showed an increased cancer incidence and mortality among firefighters and mesothelioma; however, data beyond a summary risk estimate was not provided in-text or in the supplementary information, and the CI was not provided for mortality. The study authors did not detail limitations of their study of the datasets they used. There were a large number of cancers assessed in this meta-analysis, elevated SIREs or SMREs were also found for the following cancer sites: Colon Rectal Prostate Testis Thyroid Pleura Melanoma NHL

Evidence for the Independent Panel's review				
	Laroche, and L'Esperance (2021) **Study type:** Systematic review of 11 systematic reviews, 1 of which related to mesothelioma (Jalilian 2019 – above) **Comparator:** Cancer incidence and mortality among firefighters compared to the general population. **Countries:** Not provided, though likely similar to the countries listed above.	Population Not provided Methods Databases searched included MEDLINE (PubMed), Embase, Cochrane Library, Centre for Reviews and Dissemination, Web of Science, CINAHL, PsycNet, ABI/INFORM Global and SCOPUS. Search dates were from the inception of the database up to 12 October 2019. The methodological quality of the systematic reviews included were assessed using the ROBIS tool. This review was performed according to the PRISMA statement.	Incidence of mesothelioma in firefighters risk estimates: SIRE: 1.60 (95% CI: 1.09, 2.34) Only statistical data for mesothelioma provided was from Jalilian 2019 (above) though in the discussion another Australian descriptive study (Guidotti, 2014) was discussed as finding a strong positive association between mesothelioma and firefighting.	A significant increase of the incidence or risk of mesothelioma was found for firefighters compared to the general population. Only a small number of studies cited support this statement, but the results are strong and consistent A large number of cancers assessed in this review, elevated cancer incidences in firefighters was found for: Rectal Prostate Testicular Mesothelioma Melanoma Elevated cancer mortality in firefighters was found for rectal and NHL.
Summary of Independent Panel's assessment				
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**		

Evidence for the Independent Panel's review		
	Strength of association	Based on the evidence presented, the Independent Panel agree that there is a strong association between firefighting and mesothelioma.
	Consistency or reproducibility	Based on the evidence presented, the Independent Panel agree that the association between firefighting and mesothelioma has been consistently reproduced.
	Specificity	The relationship between firefighting and mesothelioma is well defined.
	Temporality or time sequence	Mesothelioma occurs after firefighting exposure.[25]
	Biological gradient	Yes, there is a dose-response relationship between firefighting and mesothelioma.[25]
	Biological plausibility	Yes, it is plausible that firefighting can cause mesothelioma.[25]
	Coherence	Synthesis of evidence presented above, concludes there is sufficient evidence of the causal connection between firefighting and mesothelioma.[25,27,29,30]
	Analogy	Not applicable for this exposure/disease pairing.
	Experimental evidence (if relevant)	Not applicable for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on the evidence presented, the Independent Panel agree that there is a sufficiently strong causal connection between firefighting and mesothelioma. The Panel notes that occupations are a broader exposure categorisation than what is currently listed on Schedule 2, however, the evidence highlights that is not possible to distinguish individual elements agents that might be causal.
	Proportion of work cases	ACC does not have current data about the proportion of work-related mesothelioma claims with a link to firefighting. No independent exposure data for Aotearoa New Zealand was found in the published peer-reviewed literature.
Independent Panel recommendation	**Recommend inclusion on Schedule 2**	

Evidence for the Independent Panel's review	
Suggested wording to incorporate into Schedule 2	Amend entry 33: **"**Bladder carcinoma diagnosed caused by 2-naphthylamine, benzidine, 4-aminobiphenyl, N, N-Bis (2-chloroethyl)-2-naphthylamine, other aromatic amines, poly-cyclic aromatic hydrocarbons, or firefighting."**

2.2.7 Trichloroethylene and kidney cancer

Evidence for the Independent Panel's review				
Exposure	Trichloroethylene			
Related diseases	Kidney cancer			
Summary statement	Sufficient causal evidence			
ILO guidance notes	Kidney cancer caused by trichloroethylene is listed. "There is sufficient evidence in humans for the carcinogenicity of trichloroethylene in causing cancer of the kidney. Trichloroethylene has been classified as carcinogenic to humans by IARC (Group 1). Kidney, or renal cancer refers to any type of cancer that involves the kidney, and mainly originates in two parts of the kidney, the renal tubule, and the renal pelvis."[1]			
IARC advice	The re-evaluation of trichloroethylene by IARC in 2012 resulted in a new classification in Group 1, *carcinogenic to humans*, based on sufficient epidemiological evidence for cancer of the kidney, with string mechanistic support from studies in experimental animals and exposed humans.[31]			
NIOSH advice	NIOSH states that there is convincing evidence that trichloroethylene can cause kidney cancer. "Lifetime exposure to trichloroethylene resulted in increased liver cancer in mice and increased kidney cancer in rats at relatively high exposure levels. The Department of Human Health Services (HHS) has classified trichloroethylene as "*known to be a human carcinogen*" based on sufficient evidence of carcinogenicity from humans. Similarly, the International Agency for Research on Cancer (IARC) has classified it as "carcinogenic to humans" and EPA has characterized it as "carcinogenic in humans by all routes of exposure." These agencies concluded that there was sufficient evidence from human studies that trichloroethylene exposure can cause kidney cancer in humans. There is also some evidence of an association between trichloroethylene exposure and non-Hodgkin's lymphoma in humans."[32]			
Deemed Diseases List advice	Renal/kidney cancer caused by trichloroethylene is listed.			
Existing Schedule 2 entry	Chronic solvent-induced encephalopathy and peripheral neuropathy caused by trichloroethylene are listed.			
Evidence from academic literature	Summary of evidence search: two meta-analyses met the inclusion criteria (see *section 1.2.5*). These two meta-analyses were cited by IARC in 2012. The only study that met the criteria published post 2012 was a review of the same studies identified in the below meta-analyses.			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

Evidence for the Independent Panel's review				
	Karami, S., et al (2012)[33] **Study type:** Meta-analysis of 28 studies, 20 of which were relevant to trichloroethylene exposure (10 cohort and 10 case-control) **Comparator:** Expected/observed cases and unexposed/exposed subjects (dependant on the study data provided). **Countries:** Sweden. Finland. Germany, United States, Denmark, Taiwan, United Kingdom, Canada, France,	Pooled population: Study participants: 225,823 Total number of pooled kidney cancer cases: 502 Gender and ethnicity data not provided. Methods: Database searched was PubMed. Studies published from 1950 to 2011 were included I the meta-analysis. Statistical model used was random effects model. Higgin's I^2 statistic and Cochrane's Q test were used to statistically evaluate sources of heterogeneity across studies.	Cohort and case–control studies combined that specifically assessed trichloroethylene exposure after excluding outlier studies that contributed to heterogeneity: RR: 1.32 (95% CI: 1.17, 1.50) Cohort studies: RR: 1.26 (95% CI: 1.02, 1.56 Case–control studies: OR: 1.35 (95% CI: 1.17, 1.57)	This study supports an association between kidney cancer and trichloroethylene. This study also assessed exposure to chlorinated solvents (as well as trichloroethylene) which were deemed not to be statistically significant. Regardless of study design, significant estimates were only observed in studies specifically assessing occupational exposure to trichloroethylene.

Evidence for the Independent Panel's review				
	Scott, C. S., & Jinot, J. (2011)[34] **Study type:** Meta-analysis 24 studies, 17 of which were relevant to kidney cancer (9 case control and 8 cohort studies) **Comparator:** Cancer incidence and mortality from trichloroethylene (including kidney, liver and NHL) compared with controls. Details of the control groups not provided – likely variable. **Countries:** Sweden, Finland, United States, Germany, France, Ireland, Italy	Pooled participants: 217,907 pooled participants. Methods: Database searched was PubMed, search date cutoff was December 2010 Models used were random-effects and fixed-effects.	Pooled kidney cancer + trichloroethylene exposure association RR: 1.58 (95% CI: 1.28, 1.96) Pooled overall cancer + trichloroethylene exposure association RR: 1.27 (95% CI: 1.13, 1.43) Relative risk is higher for kidney cancer than the overall cancer risk.	The findings of this study provide support for a causal association between trichloroethylene exposure and kidney cancer. "For kidney cancer, the elevated relative risk estimates for overall TCE exposure and the highest exposure groups in the primary and alternative analyses provide robust support for a small, statistically significant increased risk, without evidence of heterogeneity or publication bias. The lack of observed heterogeneity provides evidence of consistency in kidney cancer risk estimates from independent epidemiologic studies of different industries with high potential for TCE exposure, regardless of study design." There is some support for a connection for NHL, and limited support for a connection with liver cancer.

Summary of Independent Panel's assessment		
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**
	Strength of association	Based on the evidence presented, the Independent Panel agree that there is a strong association between trichloroethylene and kidney cancer.
	Consistency or reproducibility	Based on the evidence presented, the Independent Panel agree that the association between trichloroethylene and kidney cancer has been consistently reproduced.

Evidence for the Independent Panel's review		
	Specificity	The relationship between trichloroethylene and kidney cancer is well defined.
	Temporality or time sequence	Kidney cancer occurs after exposure to trichloroethylene.[31]
	Biological gradient	Yes, there is a dose-response relationship between trichloroethylene and kidney cancer.[31]
	Biological plausibility	Yes, it is possible that trichloroethylene causes kidney cancer.[31]
	Coherence	Synthesis of evidence presented by IARC, as well as the meta-analyses summarised above, conclude there is sufficient evidence of the causal connection between trichloroethylene and kidney cancer.[31,33,34]
	Analogy	Not applicable for this exposure/disease pairing.
	Experimental evidence (if relevant)	Not applicable for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on the evidence presented, the Independent Panel agree that there is a sufficiently strong causal connection between trichloroethylene and kidney cancer.
	Proportion of work cases	ACC does not have current data about the proportion of work-related kidney cancer and exposure to trichloroethylene No independent exposure data for Aotearoa New Zealand was found in the published peer-reviewed literature.
Independent Panel recommendation	**Recommend inclusion on Schedule 2**	
Suggested wording to incorporate into Schedule 2	New entry: Renal cancer diagnosed caused by occupational exposure to trichloroethylene. NB: use renal in new entry (not kidney) to remain consistent with Schedule 2 wording.	

2.2.8 Vinyl chloride and hepatocellular carcinoma

Evidence for the Independent Panel's review				
Exposure	Vinyl chloride			
Related diseases	Hepatocellular carcinoma (a form of primary liver cancer, different to angiosarcoma of the liver)			
Summary statement	Sufficient causal evidence			
ILO guidance notes	Hepatocellular carcinoma caused by vinyl chloride is listed. "Hepatocellular carcinoma a cancer of the hepatic cells, which is one of the most common malignancies worldwide and the most common type of liver cancer."[1]			
IARC advice	"There is sufficient evidence in humans for the carcinogenicity of vinyl chloride. Vinyl chloride causes angiosarcomas of the liver and hepatocellular carcinomas."[21]			
Deemed Diseases List advice	Primary malignant disease of the liver caused by vinyl chloride monomer is listed.			
Existing Schedule 2 entry	Angiosarcoma of the liver diagnosed caused by vinyl chloride monomer is listed.			
Evidence from academic literature	Summary of evidence search: one review was returned that met the inclusion criteria (see *section 1.2.5*).			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

	Fedeli, U., et al. (2019)[35] **Study type:** Review of 5 studies (3 cohort, 2 nested case-control). **Comparator:** Cumulative exposure (ppm-years) used as assessment for 4 of the 5 studies, for 1 type of exposure was the comparator (Wong). **Countries:** United States, Europe, and Taiwan	Pooled population of all study participants: 24,574 Cases n: 103 Methods: Methodology of review was not specified	RR of association between HCC and occupational exposure to VCM Ward (2001) Exposure <734 ppm-years 1.0 *NB: no CI given* Exposure 735-2379 ppm-years 3.02 (95% CI: 0.50, 1.81) Exposure 2380-5188 ppm-years 2.47 (95% CI: 0.26, 23.9) Exposure 5189-7531 ppm-years 5.33 (95% CI: 0.54, 52.8) Exposure ≥7532 ppm-years 20.3 (95% CI: 2.98, 138) Mundt (2017) Exposure <1021 ppm-years 1.0 *NB: no CI given* Exposure 1022-3300 ppm-years 1.2 (95% CI: 0.4, 3.8) Exposure 3301, 5685 ppm-years 7.2 (95% CI: 2.6, 20.0) Exposure 5686-10,551 ppm-years 7.3 (95% CI: 2.5, 21.1) Exposure ≥ 10552 18.8 (95% CI: 6.8, 51.9)	The study authors conclude that available original studies reviewed by IARC and published after IARC's assessment confirmed the association between occupational vinyl chloride monomer exposure and hepatocellular carcinoma. "All the original studies available provide compelling evidence of the causal role of occupational VCM exposure in the development of HCC." Background: The role of occupational exposure to VCM in the development of angiosarcoma of the liver is well known since the mid-1970s. In 2007 IARC established that exposure to VCM causes both ASL and HCC; however, some controversy remained because findings on HCC were based only on a limited number of confirmed cases.

Evidence for the Independent Panel's review				
			Fedeli (2019) Exposure <734 ppm-years *NB: no CI given* Exposure 735-2379 ppm-years 1.72 (95% CI: 0.55, 5.32) Exposure 2380-5188 ppm-years 5.24 (95% CI: 2.20, 12.5) Exposure ≥ 5189 5.52 (95% CI: 2.03, 14.9) Wong (2003) Tank cleaning jobs 3.6 (95% CI: 1.4, 9.2) High-exposure jobs 2.9 (95% CI: 1.1, 7.3) Mastrangelo (2004) 1.71 (95% CI: 1.29, 2.44) alcohol/virus adjusted Escalating cumulative exposure not provided for Mastrangelo.	
Summary of Independent Panel's assessment				
Independent Panel comment against criteria	**Criterion**	**Independent Panel comment against each criterion**		
	Strength of association	Based on the evidence presented, the Independent Panel agree that there is a strong association between vinyl chloride and hepatocellular carcinoma.		

Evidence for the Independent Panel's review		
	Consistency or reproducibility	Based on the evidence presented, the Independent Panel agree that the association between vinyl chloride and hepatocellular carcinoma has been consistently reproduced.
	Specificity	The relationship between vinyl chloride and hepatocellular carcinoma is well defined.
	Temporality or time sequence	Hepatocellular carcinoma occurs after exposure to vinyl chloride.[21]
	Biological gradient	Yes, there is a dose-response relationship between vinyl chloride and hepatocellular carcinoma.[21]
	Biological plausibility	Yes, it is plausible that vinyl chloride causes hepatocellular carcinoma.[21]
	Coherence	Synthesis of evidence presented by IARC, as well as the systematic review summarised above, conclude there is sufficient evidence of the causal connection between vinyl chloride and hepatocellular carcinoma.
	Analogy	Angiosarcoma of the liver caused by vinyl chloride is listed on Schedule 2, adding hepatocellular carcinoma is an extension of the liver cancer-vinyl chloride connection.
	Experimental evidence (if relevant)	Not applicable for this exposure/disease pairing.
	Sufficiently strong causal evidence	Based on the evidence presented, the Independent Panel agree that there is a sufficiently strong causal connection between vinyl chloride and hepatocellular carcinoma.
	Proportion of work cases	ACC does not have current data about the proportion of work-related hepatocellular carcinoma claims with a link to vinyl chloride exposure. No independent exposure data for Aotearoa New Zealand was found in the published peer-reviewed literature.
Independent Panel recommendation	**Recommend inclusion on Schedule 2**	
Suggested wording to incorporate into Schedule 2	Amend entry 21: "Angiosarcoma, or hepatocellular carcinoma of the liver diagnosed caused by vinyl chloride monomer."	

2.2.9 Cover for future pandemics

Early on we established that it would not be practical to include Covid-19 as a disease on Schedule 2; however, the Independent Panel feel it is important for Schedule 2 to have some coverage for particularly exposed populations in the event of future pandemics. The Independent Panel spent time discussing the appropriateness, and the specific of wording of a potential Schedule 2 entry that would cover pandemic-related disease in some limited circumstances. We understand the potential implications of including such an entry, but on the advice of the Independent Panel, encourage MBIE to consider whether the below (or something similar) may be appropriate to incorporate in Schedule 2:

> *Pandemic communicable disease diagnosed by an accepted laboratory test in frontline workers during lockdown conditions*.

If MBIE or ACC were to move forward with such a provision, we recommend seeking legal advice and/or conducting an evidence review to inform the best approach.

2.3 Exposure/disease pairings to monitor

Some exposure/disease pairings had limited evidence of causality at present; however, the Independent Panel considered that such evidence is developing and it will be important to reconsider the evidence underpinning the pairings as it evolves. These exposure/disease pairings could be considered in future reviews of Schedule 2. The exposure/disease pairings are summarised in the table below.

Exposure/disease	Advice from the independent Panel
Asbestos and cholangiocarcinoma	Through the evidence review for 1,2 dichloropropane and cholangiocarcinoma (bile duct cancer), some limited evidence was identified that suggested a potential link between asbestos and cholangiocarcinoma. This exposure/disease pair should be re-examined at the next review of Schedule 2.
Carcinogenic effects of cadmium	The panel considered the connection between cadmium and kidney cancer, but the evidence has insufficient strength at this point in time. The biological mechanism of carcinogen concentration in the prostate is unclear, but it would be useful to maintain a watching brief as the evidence develops.
Coal tar pitch and bladder cancer	Evidence of this connection is limited but emerging. It is not yet sufficiently convincing to enable a recommendation for inclusion on Schedule 2.
Coal tar pitch and kidney cancer	Evidence of this connection is limited but emerging. It is not yet sufficiently convincing to enable a recommendation for inclusion on Schedule 2.
Formaldehyde and endometriosis	As part of our commitment to apply an intersectional and gender-equity lens on this work, we investigated what emerging evidence existed for female-specific occupational diseases that might otherwise be missed in the core advisory papers (ILO, DDL etc). As such, we have identified that there is emerging evidence of a connection between shift work and formaldehyde and endometriosis, and recommend this connection be re-examined at the next Schedule 2 review. There are some reports of a connection between formaldehyde and endometriosis (including a 1999 Finish cohort study and 2011 systematic review) but more robust testing of this association with more conclusive results are required to establish causality.
Formaldehyde and leukaemia	IARC has connected this exposure and disease; however, the evidence on which that decision was based has been contested. The independent Panel did not think that the evidence was convincing to the point of causality. New evidence may emerge which could provide a more compelling case.

Exposure/disease	Advice from the independent Panel
Nickel and asthma	There is a known association between metals and asthma, but there is limited epidemiological evidence to support the connection between nickel and asthma at this time.
Platinum and asthma	There is a known association between metals and asthma, but there is limited epidemiological evidence to support the connection between platinum and asthma at this time.
Polycyclic aromatic hydrocarbons (PAH) and skin cancer	There is emerging evidence specific to PAH's and skin cancer, however there is some further investigative work required to better understand the connection between PAH and tar and pitch, and the impact of this connection on future Schedule 2 reviews. As an element of tar and pitch, PAH and skin cancer has some coverage under item 15 (skin cancer caused by tar, pitch, or their residues).
Shift work and breast cancer	As part of our commitment to apply an intersectional and gender-equity lens on this work, we investigated what emerging evidence existed for female-specific occupational diseases that might otherwise be missed in the core advisory papers (ILO, DDL etc). as such, we have identified that there is emerging evidence of a connection between shift work and breast cancer, and recommend this connection be re-examined at the next Schedule 2 review.
Vanadium and asthma	There is a known association between metals and asthma, but there is limited epidemiological evidence to support the connection between vanadium and asthma at this time.

2.4 Exposure/disease pairings that should not be included on Schedule 2

The following exposure/disease pairings (2.4.1 – 2.4.9) were further investigated after the first Independent Panel meeting, but the Independent Panel assessed that the evidence available did not provide a strong enough basis for causality at this time and have thus been excluded from inclusion for this review. The evidence (where available) has been provided in the tables below; however, for several of the exposure/disease pairings in this category, there was limited and/or poor evidence which did not meet our evidence inclusion criteria.

For these exposure/disease pairings, there is emerging evidence of causality and have therefore been included in **section 2.3** exposure/disease pairings to monitor.

- **Cadmium and kidney cancer**
- **Coal tar and pitches and bladder cancer**
- **Coal tar and pitches and renal cancer**
- **Formaldehyde and leukaemia**
- **Nickel (or its compounds) and asthma**
- **Platinum (or its compounds) sensitiser asthma**
- **Polycyclic aromatic hydrocarbons and non-melanoma skin cancers**
- **Thallium and polyneuropathy**
- **Vanadium (or its compounds) and asthma**

2.4.1 Cadmium and kidney cancer

Evidence for the Independent Panel's review				
Exposure	Cadmium			
Related diseases	Kidney cancer			
Summary statement	Insufficient causal evidence			
ILO guidance notes	Cadmium and kidney cancer is not officially designated by ILO as a causative relationship: "Cadmium and cadmium compounds cause cancer of the lung. Positive associations have been observed between exposure to cadmium and cadmium compounds and cancer of the kidney and of the prostate."[1]			
IARC advice	Cadmium and cadmium compounds are considered carcinogenic to humans (Group 1);[36] however, IARC has stated that there is only limited evidence that cadmium causes kidney cancer specifically.[37]			
NIOSH advice	Prostate and lung cancer listed as cancer sites related to cadmium, kidney cancer not listed.[38]			
Deemed Diseases List advice	Cadmium is not listed as an associated exposure to kidney cancer on the Deemed Diseases List but cadmium is listed in connection to lung cancer.			
Existing Schedule 2 entry	Cadmium is not listed as an associated exposure to kidney cancer on the Schedule 2 but is listed in connection to lung cancer and chronic renal failure.			
Evidence from academic literature	Summary of evidence search: one meta-analysis met the inclusion criteria (see *section 1.2.5*).			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

Evidence for the Independent Panel's review				
	Song, J.K., et al. (2015)[39] **Study type:** Meta-analysis of 9 studies including 7 case-control studies, 1 nested case-control study, and 1 prospective cohort study. **Comparator:** Cases of renal cancer in occupational populations exposed to cadmium. **Countries:** Europe and North America.	Pooled population: 24,896 total pooled participants with 6038 kidney cancer cases. Male and female subjects, though n for males and females not provided. Data on ethnicity not provided Methods: Databases searched include PubMed and Embase. Random and fixed effects models were used. Low heterogeneity was observed.	Association between cadmium exposure and renal cancer risk (n=number of studies) Overall OR: 1.47 (95% CI: 1.27, 1.71) Case-control (n=9) OR: 1.47 (95% CI: 1.26, 1.72) Cohort (n=1) OR: 1.39 (95% CI: 0.43, 4.52) Men (n=3) OR: 1.4 (95% CI: 1.16, 1.69) Women (n=3) OR: 1.64 (95% CI: 1.09, 2.47)	The meta-analysis showed that a high cadmium exposure significantly increased renal cancer risk. The association remained consistent when stratified by geographic region and gender; however, mixed results were produced when stratified by sample size, study design, NOS score, adjustment for covariates, effects measure, and exposure type.
Summary of Independent Panel's assessment				
There is limited evidence for causality, as highlighted by IARC. The Independent Panel does not recommend cadmium and kidney cancer be added to Schedule 2 at this time. It recommends that MBIE monitor the emerging evidence and prioritise this exposure/disease pairing at the next review of Schedule 2.				
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**			

2.4.2 Coal tar pitches and bladder cancer

Evidence for the Independent Panel's review	
Exposure	Coal tar pitch
Related diseases	Bladder cancer
Summary statement	Insufficient causal evidence
ILO guidance notes	ILO state that coal tar pitches cause skin and lung cancer, but do not mention bladder cancer.
IARC advice	IARC states that there is sufficient evidence for a causal relationship between coal-tar pitch and lung cancer but that there is only limited evidence for a relationship between coal-tar pitch and bladder cancer. "There is *sufficient evidence* in humans for the carcinogenicity of occupational exposures during paving and roofing with coal-tar pitch. An increased mortality from urinary or bladder cancer was observed in one or more of cohort study, but this finding was not widely supported by other studies."[40]
Deemed Diseases List advice	Lung and skin cancer only caused by coal-tar pitch is listed.
Existing Schedule 2 entry	Skin cancer caused by tar or pitch is listed.
Evidence from academic literature	Summary of evidence search: no returns met the inclusion criteria (see *section 1.2.5*). When searching for evidence on coal-tar pitches, there were some results returned regarding PAHs, but causality specifically to coal-tar pitches was unclear. Future investigations into coal-tar pitches, PAHs, and coke oven emissions should invest resources into better investigating the link between these exposes and the diseases impacts the present individually or collectively.
Summary of Independent Panel's assessment	
There is limited evidence for causality, as highlighted by IARC. The Independent Panel does not recommend coal tar pitch and renal cancer be added to Schedule 2 at this time. It recommends that MBIE monitor the emerging evidence and prioritise this exposure/disease pairing at the next review of Schedule 2.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.3 Coal tar pitches and renal cancer

Evidence for the Independent Panel's review	
Exposure	Coal tar pitch
Related diseases	Kidney/renal cancer
Summary statement	Insufficient causal evidence
ILO guidance notes	ILO state that coal tar pitches cause skin and lung cancer, but do not mention renal cancer.
IARC advice	IARC states that there is sufficient evidence for a causal relationship between coal-tar pitch and lung cancer but it does not make any connection between coal-tar pitch and kidney cancer. "There is *sufficient evidence* in humans for the carcinogenicity of occupational exposures during paving and roofing with coal-tar pitch. An increased mortality from urinary or bladder cancer was observed in one or more of cohort study, but this finding was not widely supported by other studies."[40]
NIOSH advice	Not found.
US Department of Health and Human Services advice	There is a known association between coat-tars and skin cancer and there are some reports of an association with lung, kidney, bladder and digestive tract cancers.[41]
Deemed Diseases List advice	Lung and skin cancer caused by coal-tar pitch is listed.
Existing Schedule 2 entry	Skin cancer caused by tar or pitch is listed.
Summary of Independent Panel's assessment	
There is limited evidence for causality, as highlighted by IARC. The Independent Panel does not recommend coal tar pitch and renal cancer be added to Schedule 2 at this time. It recommends that MBIE monitor the emerging evidence and prioritise this exposure/disease pairing at the next review of Schedule 2.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.4 Formaldehyde and leukaemia

Evidence for the Independent Panel's review	
Exposure	Formaldehyde (inhalation)
Related diseases	Leukaemia
Summary statement	Insufficient causal evidence
ILO guidance notes	Formaldehyde and leukaemia are not linked by the ILO.
IARC advice	A 2012 Working Group "concluded that the epidemiologic evidence shows that occupational exposure to formaldehyde causes leukaemia"; however, Monograph 100F noted that this determination was not unanimous, and a small majority viewed the evidence as sufficient of carcinogenicity while a minority viewed the evidence as limited. IARC further stated that: "Particularly relevant to the discussions regarding sufficient evidence was a recent study accepted for publication which, for the first time, reported aneuploidy in blood of exposed workers characteristic of myeloid leukaemia and myelodysplastic syndromes, with supporting information suggesting a decrease in the major circulating blood-cell types and in circulating haematological precursor cells [referring to Zhang, 2010]. The authors and Working Group felt that this study needed to be replicated."[42]
NIOSH advice	NIOSH list nasal cancer as the relevant cancer site, no mention of leukaemia.[43]
Deemed Diseases List advice	Leukaemia caused by formaldehyde is listed.
Existing Schedule 2 entry	Only naso-pharyngeal carcinoma caused by leukaemia is listed.
	Summary of evidence search: a total of four returns met the inclusion criteria (see *section 1.2.5*). An umbrella review, systematic review, linear regression analysis and cross-sectional study are summarised below. Despite IARC classifying formaldehyde as an occupational cause of leukaemia in 2012, there still seems to be some contention around this connection. **Background:** Zhang et al. (2010) was influential in IARC's decision that formaldehyde exposure may cause leukaemia. This recognition came despite the fact that primary evaluations reported by Zhang et al. (2010) of aneuploidies and indicators of haematotoxicity were limited to fairly crude aggregation of workers from different industries into "exposed" and "unexposed" categories. Other major criticisms of the Zhang et al. (2010) were the decision not to present any results by estimated individual exposure level, which would have provided a fuller evaluation and stronger evidence of an association, should one exist. Also, key limitations in the data collection (whether the reported aneuploidies could have occurred during cell culture in vitro) were not reported by the original authors.

Evidence for the Independent Panel's review				
	Study details	**Population and methods**	**Relevant data points**	**Notes**

	La Torre, G., et al. (2023)[44] **Study type:** Umbrella review of 15 articles (1 meta-analysis, 1 cross-sectional study and 13 case-control or cohort studies) investigating the association between formaldehyde and leukaemia. **Comparator:** Formaldehyde and irritant diseases AND formaldehyde and neoplastic diseases (of which leukaemia is one). **Country:** Not provided.	Pooled population: 955,258 study participants Data on ethnicity and gender not provided. Methods: Databases searched included PubMed, Scopus and Web of Science published between 2010 - 2020 Data extraction and quality assessment were performed according to Assessing the Methodological Quality of Systematic Reviews (AMSTAR) score.	Some included studies assessed several cancers but did not report data separately: interpret with caution. Bachand et al. (2010) – high quality score (nasopharyngeal cancer (NPC), leukaemia) OR: 1.10 (95% CI: 0.80, 1.50) *Weak association, null included in CI.* Nilsen et al. (2010) – low quality score (NPC, leukaemia) RR: 1.33 (95% CI: 0.69, 2.56) *Weak association, null included in CI.* Golden (2011) – critically low quality score (NPC, leukaemia) RR: 0.72 (95% CI: 0.40, 1.28) *Weak association, null included in CI and r.* Checkoway et al. (2012) – low quality score (leukaemia) Myeloid leukaemia RR: 1.78 (95% CI: 0.87, 3.64) *Weak association, null included in CI.* Other (non-myeloid) leukaemia RR: 1.42 (95% CI: 0.92, 2.18) *Weak association, null included in CI.* Gentry et al. (2013) – low quality score (leukaemia) p=.10 *Weak correlation, only p value provided.* Polychronakis et al. (2013) – high quality score (leukaemia) RR: 1.37 (95% CI: 1.03, 1.81) *Weak association*	Weak association reported between leukaemia and formaldehyde. 33 percent of the articles reviewed (5 out of 15) supported the association between formaldehyde exposure and leukaemia/lymphoma. Limitations noted by the authors regarding the reviewed studies: specific populations that do not always align (eg, children, occupationally exposed workers) small population groups, in some cases – a high risk of bias ethnicity and gender not provided in most studies.

Evidence for the Independent Panel's review				
			Charbotel et al. (2014) – low quality score (leukaemia) OR: 2.47 (95% CI: 1.42, 4.27) *Good association.* Albertini et al. (2016) – low quality score (leukaemia, lymphoma) RR: 1.31 (95% CI: 1.07, 1.60) *Good association.* Chappell et al. (2016) – low quality score (NPC, leukaemia) r: 0.384; P 0.001 *Good correlation* Nielsen et al. (2017) – critically low quality score (leukaemia) RR: 1.15 (95% CI: 0.97, 1.36) p<.05 *Good correlation, NB null included in CI.* Mundt et al. (2017) – low quality score (myeloid leukaemia) OR: 0.80 (95% CI: 0.70, 0.92) *Weak association, NB null included in CI.* Allegra et al. (2019) – low quality score(acute myeloid leukaemia) OR: 2.45 (95% CI: 1.32, 4.52) *Good association* Shallis et al. (2020) – low quality score (acute myeloid leukaemia) RR: 1.42 (95% CI: 0.9-2.18) *Weak association*	

Evidence for the Independent Panel's review				
	Allegra et al. (2019)[45] **Study type:** Systematic review of 5 studies (1 cohort study, 1 molecular epidemiological study, 1 data reanalysis, 1 qualitative risk analysis and 1 literature review). **Comparator:** Exposed/unexposed to formaldehyde **Countries:** United states, China **NB:** a lot of data was not provided in-text for this review and supplementary information was not able to be located.	Pooled population: 25,764 study participants Data on ethnicity and gender not provided. Methods: Seach of PubMed and Embase databases up to 28 May 2018. Results were tested against criteria, but authors do not provide these. No further information on quality assessment was provided.	Data from studies included in this review is below where provided. Some of these were also included in the review above. Checkoway et al. Subjects with total exposures of 0.5 to less than 2.5 ppm–years HR: 2.44 (95% CI: 1.08, 5.51) Subjects with 2.5 ppm–years or more HR: 2.49 (95% CI: 1.13, 5.49) p=.04 *Conclusion:* No overall association, though a not statistically significant risk was detected for those working one year or more. Zhang et al. *Data:* not provided in this review but Zhang study detailed below. *Conclusion:* Leukaemia induction by formaldehyde is biologically plausible. Gentry et al. *Data:* not provided *Conclusions:* No association Jones et al. *Data:* not provided *Conclusions:* No association Charbotel et al. *Data:* not provided *Conclusions:* Association – though the only data that supports this connection is Zhang's data, which has subsequently been questioned.	Review does not support the hypothesis that formaldehyde is a cause of acute myeloid leukaemia. The aim of the present study was to evaluate associations between cumulative and peak formaldehyde exposure and occurrence of acute myeloid leukaemia. The review uncovered several methodological inconsistencies with Zhang's work, highlighted by Gentry. Aneuploidy of some chromosomes occurring in vivo in hematopoietic stem cells in human subjects exposed to formaldehyde has not been proved. No constant statistically significant association between formaldehyde exposure and chromosome aberrations.

	Mundt et al (2017)[46] **Study type:** Linear regression analysis of Zhang 2010 data. **Comparator:** Blood cell counts on exposed to formaldehyde/ unexposed controls. **Country:** China	Population: 94 workers in China, 43 exposed to formaldehyde and 51 frequency-matched controls (from Zhang 2010). 13 women 81 men All participants were Chinese. Methods: (from Zhang data). Complete blood counts with differential and lymphocyte subsets were measured for each study subject. Each of the blood count parameters, specifically, white blood cell (WBC) count and its component lymphocytes, monocytes, and granulocytes; red blood cell (RBC) count and its component haemoglobin and platelets; and mean corpuscular volume (MCV), was	**Table 1.** Association between formaldehyde exposure and the blood parameters. | Blood parameter	Unadjusted Exp(β[a])	95% CI	*p* value	Adjusted Exp(β[a])[b]	95% CI	*p*[c] value
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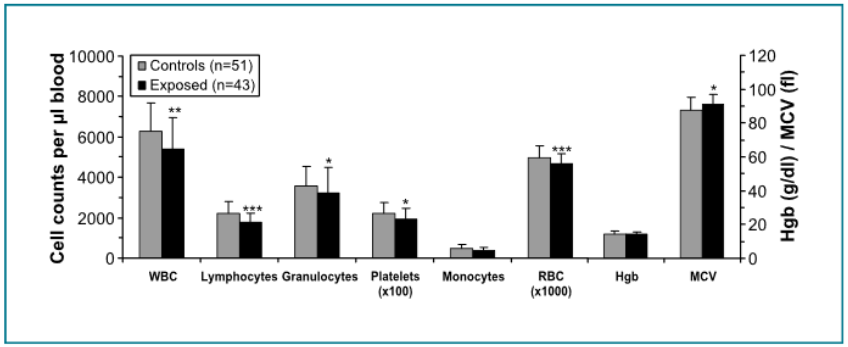
WBC						
Unexposed	Reference			Reference		
<1.3 ppm	**0.85**[d]	0.76–0.96		**0.87**	0.78–0.97	
≥1.3 ppm	**0.86**	0.76–0.97	.992	**0.85**	0.76–0.96	.943
Lymphocytes						
Unexposed	Reference			Reference		
<1.3 ppm	**0.83**	0.73–0.95		**0.85**	0.75–0.96	
≥1.3 ppm	**0.80**	0.70–0.92	.890	**0.79**	0.69–0.90	.660
Monocytes						
Unexposed	Reference			Reference		
<1.3 ppm	0.86	0.72–1.04		0.90	0.77–1.06	
≥1.3 ppm	0.92	0.76–1.11	.856	0.89	0.75–1.04	.973
Granulocytes						
Unexposed	Reference			Reference		
<1.3 ppm	**0.86**	0.74–1.00		0.87	0.75–1.01	
≥1.3 ppm	0.89	0.76–1.04	.931	0.88	0.75–1.03	.997
RBC						
Unexposed	Reference			Reference		
<1.3 ppm	**0.94**	0.89–0.99		**0.94**	0.91–0.98	
≥1.3 ppm	**0.94**	0.89–1.00	.999	**0.94**	0.90–0.98	.947
Hemoglobin						
Unexposed	Reference			Reference		
<1.3 ppm	0.97	0.92–1.02		0.98	0.94–1.01	
≥1.3 ppm	1.00	0.94–1.05	.667	0.99	0.95–1.03	.818
Platelets						
Unexposed	Reference			Reference		
<1.3 ppm	**0.85**	0.76–0.96		**0.85**	0.75–0.96	
≥1.3 ppm	0.91	0.80–1.03	.695	0.91	0.80–1.03	.674
MCV						
Unexposed	Reference			Reference		
<1.3 ppm	1.03	0.99–1.07		1.03	0.99–1.08	
≥1.3 ppm	**1.06**	1.02–1.11	.379	**1.06**	1.02–1.11	.550	 [a]Regression coefficient between log-transformed blood parameter and formaldehyde. [b]Adjusted for combined sex/smoking variable. [c]*p* values for pairwise comparison between <1.3 ppm and ≥1.3 ppm categories. [d]Bolded results are statistically significantly different from the reference group. .	No association found. While Zhang et al. (2010) has been cited heavily to support the biological plausibility of formaldehyde as a cause of human leukaemia, fuller analysis of the original study data verifies methodological limitations and demonstrating no association between individual exposure levels and several blood parameters among those occupationally exposed to formaldehyde. Zhang et al. did not follow their own study protocol eg, few subjects had adequate numbers of CFU-GM progenitor cells analysed to meet the study protocol criteria of evaluating >150 cells. "The lack of compliance with the study protocol is critical, as the cutoff or background for FISH results is expected to be above zero and no cutoff was established for this analysis. When considering the protocol established by Zhang et al. (2010), for monosomy 7,

Evidence for the Independent Panel's review				
		examined as the primary outcome variables of interest. (from this analysis) Exposure values for each worker were linked with the eight blood count parameters and, where applicable, the aneuploidy results, and compared between exposed/unexposed. Additionally, blood parameters were compared to reference intervals for the Chinese population All analyses were conducted using SAS 9.3.		only a single exposed worker and four controls met the criterion of scoring 150 cells, while for trisomy 8, only three exposed workers and three controls met the criterion."

Evidence for the Independent Panel's review				
	Zhang et al (2010)[47] **Study type:** Cross-sectional study **Comparator**: Blood cell counts on exposed to formaldehyde/ unexposed controls. **Country:** China	Population: 94 workers in China, 43 exposed to formaldehyde and 51 frequency-matched controls. 13 women 81 men All participants were Chinese. Methods: Measuring complete blood counts and peripheral stem/progenitor cell colony formation of exposed participants compared to controls.	Lower white blood cell counts in exposed population: p=.0016. Lower lymphocyte count in exposed populations: Pp=.0002. Frequency of monosomy (loss) of chromosome 7 in formaldehyde-exposed workers was significantly elevated: p=.0039. Frequency of trisomy 8 (gain) had a 4-fold significant increase p=.040. Formaldehyde exposure was, therefore, associated with an increase in leukaemia-specific chromosomal aneuploidy in the hematopoietic progenitor cells of the exposed workers. See graph below taken directly from Zhang et al.	Significant association found. The objective of this study was to determine if formaldehyde exposure disrupts hematopoietic function and produces leukaemia-related chromosome changes in exposed humans. "Among exposed workers, peripheral blood cell counts were significantly lowered in a manner consistent with toxic effects on the bone marrow and leukaemia-specific chromosome changes were significantly elevated in myeloid blood progenitor cells. These findings suggest that formaldehyde exposure can have an adverse effect on the hematopoietic system and that leukaemia induction by formaldehyde is biologically plausible, which heightens concerns about its leukemogenic potential from occupational and environmental exposures."

Evidence for the Independent Panel's review			
			 **Figure 1.** Myeloid, erythroid, and lymphocyte blood cell counts in formaldehyde-exposed and unexposed workers. A total of 43 workers exposed to formaldehyde and 51 controls were studied. Differences in cell counts (mean ± SD) were tested by linear regression, adjusting for relevant covariates as indicated in Materials and Methods. *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$. Hgb, hemoglobin (in g/dL); MCV, mean corpuscular volume (fL).
Summary of Independent Panel's assessment			
Despite IARC stating there is a connection between formaldehyde and leukaemia, the evidence published subsequently has relitigated this conclusion, and causality is therefore unclear. As such, the Independent Panel does not recommend formaldehyde and leukaemia be added to Schedule 2 at this time. It recommends that MBIE monitor the emerging evidence and prioritise this exposure/disease pairing at the next review of Schedule 2.			
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**		

2.4.5 Nickel and asthma

Evidence for the Independent Panel's review				
Exposure	Nickel (soluble, and nickel oxide fumes, largely from welding)			
Related diseases	Asthma			
Summary statement	Insufficient causal evidence			
ILO guidance notes	Asthma as possibly caused by nickel exposure is listed. "There is some evidence that inhalation of soluble nickel and of nickel oxide fumes in the welding of nickel-containing alloys can cause asthma. Following sensitization to nickel, some cases of eosinophilic pneumonitis have been observed. Nickel asthma is often associated with urticarial (acute wheals and flare skin reactions) and allergic contact dermatitis."[1]			
IARC advice	Not relevant for this disease (not cancer).			
NIOSH advice	NIOSH note in their nickel pocket-guide that inhalation of nickel can lead to allergic asthma symptoms.			
National Centre for Biotechnology Information advice	NCBI note that chronic nickel exposure, via nickel dust or aerosol inhalation, can cause asthma (among other diseases).[48] In this article NCBI do not link this statement directly to any evidence in their reference list.			
Deemed Diseases List advice	Nickel and asthma are not listed.			
Existing Schedule 2 entry	Nickel and asthma are not listed.			
Evidence from academic literature	Summary of evidence search: a total of two returns met the inclusion criteria (see *section 1.2.5*) one cohort study and one trial. There was some earlier evidence investigating nickel/asthma connection, from the 1980's and 1990's, but does not seem to be an ongoing topic of research. Both studies presented below noted that women show a higher prevalence than men to nickel allergy (not specific to asthma), potentially due to nickel presence in earrings/piercings.			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

	Kolberg et al. (2020)[49] **Study type:** Cohort study **Comparator:** Self-reported nickel allergy association with wheezing, asthma and rhinoconjunctivitis. **Country:** Germany **Background:** Kolber et al note in their introduction that previous analyses of nickel and asthma association have produced conflicting results.	Population: 2051 participants total, 1925 included in the analysis of incident asthma. Male=666 Female=912 No ethnicity data presented. Participants were identified from the population-based Study on Occupational Allergy Risks (SOLAR), a longitudinal German study following up on a 1995/96 study of asthma and allergies in childhood. SOLAR participants were contacted for follow up in 2002/03 and again in 2007-09. Methods: Questionnaire-based longitudinal study. High response rate (77.4% in 2002/03 and 70.6% in 2007-09). Outcomes analysed were incident asthma and incident wheezing	Incident asthma Males OR: 4.67 (95% CI: 1.44, 15.18) *After adjustment for pierced ears* OR: 3.19 (95% CI: 1.11, 9.11) Females OR: 0.93 (95% CI: 0.37, 2.38) *NB null included in the CI* After adjustment for pierced ears: OR: 0.96 (95% CI: 0.21, 4.33) *NB null included in the CI and OR* Incident wheezing Males OR: 2.90 (95% CI: 1.29, 6.52) After adjustment for pierced ears: OR: 2.26 (95% CI: 1.10, 4.62) Females: OR: 1.57 (95% CI: 0.96, 2.57) *NB null included in the CI*	The authors conclude that there are strong effect estimates for nickel allergy and incident wheezing in males and females; however, for females the null is included in the CI and thus this conclusion should be accepted with caution. The authors have not provided any other data to support their conclusion. There was no association of nickel allergy and asthma for females. For males, there was an association between nickel allergy and asthma; however, for pierced ears, this was no longer statistically significant after adjustment. No association was found for rhinoconjunctivitis. As this study relies on self-reported data, conclusions should be interpreted with caution. Also of note, this study did not assess occupational exposure, but exposure in the general population (despite the name of the SOLAR study).

Evidence for the Independent Panel's review				
			After adjustment for pierced ears OR: 1.27 (95% CI: 0.49, 3.27) *NB null included in the CI*	

Evidence for the Independent Panel's review				
	Brera, S., and Nicolini, A. (2005)[50] **Study type:** Trial **Intervention/comparator:** Nickel provocation test/nasal flow before and after test. **Country:** Italy NB: short report, minimal data provided.	Population: 20 patients with rhinitis, associated in 11 cases with bronchial asthma. All patients were female, aged between 24-48 years. All patients tested positive to nickel allergy via skin-prick test. No ethnicity data provided. Methods: Skin prick test for nickel allergy. Nasal provocation for nickel performed with a small piece of cotton wool impregnated with NiSO4 solution at a concentration of 10 mg/ml after a placebo test with physiological saline. Anterior active basic rhinomanometry test performed before and after nasal provocation. Student t test was used in the statistical analysis of the results.	Nasal flow in patients with nickel allergy in basal conditions and after nickel provocation test: 0.8 ± 0.1 Pa/cm2/sec. before the provocation test 0.6 ± 0.5 Pa/cm2/sec. after the provocation test Results were highly significant with p<.01.	Statistically significant difference in rhinomanometry (nasal airflow) before and after nickel nasal provocation but authors do fall short of concluding that nickel exposure causes asthma. NB: 7 out of 20 of the test subjects were allergic to nickel. Authors note that asthma (and rhinitis) due to nickel sulphate allergy have been rarely investigated in the literature, and existing evidence assesses very few (sometimes only one) cases. This study did not assess occupational exposure, but exposure to patients who had not experienced occupational nickel exposure.

Evidence for the Independent Panel's review	
Summary of Independent Panel's assessment	
The Independent Panel noted that, in their experience, most metal fumes can cause occupational asthma, though epidemiological evidence to support this is limited. As such, the Independent Panel does not recommend nickel and asthma be added to Schedule 2 at this time. It recommends that MBIE monitor the emerging evidence and prioritise this exposure/disease pairing at the next review of Schedule 2.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.6 Platinum and sensitiser asthma

Evidence for the Independent Panel's review	
Exposure	Platinum (in powder form)
Related diseases	Sensitiser asthma
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational asthma caused by platinum is listed. "Occupational exposure to platinum or its compounds can occur in the following sectors and jobs: platinum mining facilities and refineries, catalyst manufacturers and recyclers, jewellers, chemical and electronic manufacturers, the pharmaceutical industry, hospitals and healthcare facilities, and dental offices. Sensitization is characterized by a latency period – which may last from several weeks or months to, very seldom, years – between first exposure to the sensitizer at work and the development of immunologically mediated symptoms. Minimum duration for exposure is a few weeks, maximum latency period is a few months to a few years."[1]
IARC advice	Not relevant for this exposure (not cancer).
NIOSH advice	Platinum is solid in bulk form but in fine powder form can be dangerous to handle. Exposure routes are inhalation, ingestion, skin and/or eye contact and exposure symptoms include skin and respiratory irritation.[51]
Deemed Diseases List advice	No relevant entry for platinum.
Existing Schedule 2 entry	No relevant entry for platinum.
Evidence from academic literature	No relevant studies that met the inclusion criteria were found. There were a number of studies assessing the levels of platinum exposure in occupational settings in jurisdictions other than Aotearoa New Zealand, but studies specifically linking asthma and platinum exposure with a publication date within the past 10 years were not found. Some potentially relevant articles from the 1980s were identified by not reviewed in full due to their age.
Summary of Independent Panel's assessment	
The Independent Panel noted that, in their experience, most metal fumes can cause occupational asthma, though epidemiological evidence to support this is limited. As such, the Independent Panel does not recommend nickel and asthma be added to Schedule 2 at this time. It recommends that MBIE monitor the emerging evidence and prioritise this exposure/disease pairing at the next review of Schedule 2.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.7 Polycyclic aromatic hydrocarbons and non-melanoma skin-cancers

Evidence for the Independent Panel's review				
Exposure	Polycyclic aromatic hydrocarbons (PAHs)			
Related diseases	Non-melanoma skin cancers			
Summary statement	Insufficient causal evidence			
ILO guidance notes	PAHs are not listed as their own exposure by the ILO but are considered as a relevant agent in a number of exposures, eg, the section on coal tar pitch as a cause of skin cancer: *"Coal tar pitch* is a black to brown sticky paste with a characteristic odour mainly formed of a complex and poorly characterized mixture of polycyclic aromatic hydrocarbons (PAH), alkyl derivatives, nitrogen and sulphur PAH analogues and derivatives such as aromatic amines, phenols and quinones. Occupational exposures to coal tar and soot cause cancer of the skin."[1]			
IARC advice	In 2010 IARC reviewed experimental data for 60 individual PAHs in 2010. Of these 60 PAHs, one, benzo[a] pyrene, is classified as carcinogenic to humans (Group 1). IARC confirmed Group 1 carcinogenic occupational exposures related to PAHs including: coal gasification, coke production, coat-tar distillation and use, and aluminium production.[52]			
NIOSH advice	NIOSH concluded that occupational exposure to coal products can increase the risk of lung and skin cancer in workers. PAHs not specifically mentioned.[53]			
Deemed Diseases List advice	Non-melanoma skin cancer caused by PAHs is listed. This includes topical exposure from coal tar distillation, coal tar pitch, mineral oils (untreated or mildly treated), shale oils, soot (chimney sweeping).			
Existing Schedule 2 entry	Blader carcinoma caused by PAHs is listed. NB: tar and pitch (or their residues) and skin cancer is listed, Independent Panel discussion required to establish whether PAHs are included within tar/pitch.			
Evidence from academic literature	Summary of evidence search: one systematic review and one cross-sectional study met the inclusion criteria (see *section 1.2.5*).			
	Study details	**Population and methods**	**Relevant data points**	**Notes**

Evidence for the Independent Panel's review				
	Rahman, H., et al (2023)[54] **Study type:** Cross-sectional study **Comparator:** Skin cancer incidents in population compared by age group (youngest group 20-44 years used as comparator when calculating the ORs) **Country:** United States	Population: 14,716 adults from the National Health Examination and Nutrition Survey (longitudinal USA study) Gender: Female: 7,605 Male: 7,111 Ethnicity: White: 5,702 Black: 3,295 Other or mixed race: 2,264 Mexican American: 1,910 Other Hispanic: 1,545 Methods: Data was collected in three cycles: 2011, 2012, 2013-2014 and 2015-2016. Modelling used included linear logit regression models using only main effects.	Association between the six PHAs analysed and non-melanoma skin cancer 1-Hydroxynaphthalene OR: 0.64 (95% CI: 0.32, 1.29) p=.197 2-Hydroxynaphthalene OR: 1.30 (95% CI: 0.60, 2.84) p=.486 3-Hydroxyfluorene OR: 0.73 (95% CI: 0.40, 1.33) p=.283 2-Hydroxyfluorene OR: 0.67 (95% CI: 0.37, 1.20) p=.163 1-Hydroxyphenanthrene OR: 0.75 (95% CI: 0.40, 1.43) p=.368 1-Hydroxypyrene OR: 0.82 (95% CI: 0.42, 1.61) p=.547	This study found no significant association between PHAs and non-melanoma skin cancer. A marginal positive significant correlation between total arsenic and nonmelanoma was observed. This study identified a significant positive association between barium, cadmium, caesium, mercury, tin, and melanoma development.

Evidence for the Independent Panel's review				
	Weistenhöfer et al., (2022)[55] **Study type:** Systematic review of 8 epidemiological studied **Comparator:** Squamous cell carcinoma and UV radiation or PAHs. **Country:** Not specified This study referred to online supplementary information but supplementary information was not able to be found.	Population: Outdoor workers (bricklayers, civil engineers, farmers) who are exposed to UV plus tar, soot, and similar substances. N not provided. Gender and ethnicity data was not provided. Methods: Databases searched included PubMed, Web of Science, and Scopus up to August 2019. PRISMA guidelines used for this review.	Not provided in-text and supplementary information was not linked online.	Inconclusive results. "On the question of syncarcinogenesis of PAHs, only a few epidemiological studies were identified in the systematic literature search. Moreover, these did not allow for any conclusions in terms of quantifiable risks or dose-response relationships." Significant limitation on conclusions from this study given the data was not able to be accessed. Due to the applicability of the study aims to this evidence review, it has still been included.
Summary of Independent Panel's assessment				
As PAH is a residue of tar and pitch, it was determined that in many cases, skin cancer caused by PAH's would already be covered by entry 15 on Schedule 2 (*Primary epitheliomatous cancer of the skin diagnosed caused by tar, pitch, bitumen, mineral oil, anthracene, or the compounds, products, or residues of these substances*). The evidence assessed at present was inconclusive, and the Independent Panel does not recommend adding PAHs and skin cancer to Schedule 2 at this time. it recommends that MBIE monitor the emerging evidence and prioritise this exposure/disease pairing at the next review of Schedule 2.				
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**			

2.4.8 Thallium and polyneuropathy

Evidence for the Independent Panel's review	
Exposure	Thallium
Related diseases	Polyneuropathy
Summary statement	Insufficient causal evidence
ILO guidance notes	Polyneuropathy caused by acute thallium poisoning is listed. "The presentation of gastroenteritis, polyneuropathy and alopecia is regarded as the classic syndrome of thallium poisoning."[1]
IARC advice	Not relevant for this exposure (not cancer).
NIOSH advice	Exposure routes include inhalation, skin absorption, ingestion, skin and/or eye contact. Neuropathy is not listed as a symptom by NIOSH, but paraesthesia of the legs is.[56]
Deemed Diseases List advice	Thallium is included as an acute poisoning exposure and is linked to manufacturing.
Existing Schedule 2 entry	No relevant entry
Evidence from academic literature	No evidence was found that met the inclusion criteria. Some studies identified the link between thallium and neuropathy, but these were either of low-quality, or did not assess neuropathy or thallium in sufficient detail. For example, some returned papers assessed other diseases like PCOS, DNA damage and epigenetic alterations and neuropathy was listed as a possible side-effect of thallium poisoning (but was not assessed in detail). Notably, there were no relevant citations to back up this connection when cited in-text.
Summary of Independent Panel's assessment	
There was insufficient evidence of causality, with no academic evidence and little grey literature to support a connection to polyneuropathy from gradual-process exposure to thallium (thallium poisoning an accident and therefore not applicable to Schedule 2).	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.9 Vanadium and asthma

Evidence for the Independent Panel's review	
Exposure	Vanadium (inhalation of fumes or dusts)
Related diseases	Sensitiser-induced occupational asthma
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational asthma may be caused by vanadium exposure. "Occupational exposure to vanadium is possible in several production activities. Exposure to vanadium fumes, dusts and vapours can induce acute irritation of eyes, mucous membranes, skin and the respiratory tract and, in the most severe cases, acute lung injury. Exposure to vanadium, usually as vanadium pentoxide, has been reported as a possible cause of irritant-induced occupational asthma, described especially in workers engaged in maintenance of oil-fired boilers, as the fly ash produced by some types of fuel oil could be very rich in vanadium."[1]
IARC advice	Not relevant for this exposure (not cancer).
NIOSH advice	Vanadium is a powder and odourless flakes can disperse in the air. Exposure routes are inhalation, ingestion, skin and/or eye contact and exposure symptoms include irritation eyes, skin, throat; green tongue, metallic taste, eczema; cough; fine rales, wheezing, bronchitis, dyspnea (breathing difficulty).[57]
Deemed Diseases List advice	Vanadium is included as an acute poisoning exposure and is linked to manufacturing.
Existing Schedule 2 entry	No existing entry for vanadium**.**
Evidence from academic literature	No relevant studies were found. The broad PubMed search for (vanadium) AND (asthma) only returned three results and these were (1) a short overview of vanadium, (2) a short overview of metal toxicity, and (3) an assessment of whether vanadium exacerbates respiratory irritation (not causal).
Summary of Independent Panel's assessment	
The Independent Panel noted that, in their experience, most metal fumes can cause occupational asthma, though epidemiological evidence to support this is limited. As such, the Independent Panel does not recommend vanadium and asthma be added to Schedule 2 at this time. It recommends that MBIE monitor the emerging evidence and prioritise this exposure/disease pairing at the next review of Schedule 2.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

Exposure/disease pairs pairings that should not be included on Schedule 2 (no evidence reviews conducted)

The following exposure/disease pairings do not meet the intent of Schedule 2. They have a complex aetiology that is best assessed on a case-by-case basis to determine causality and exposure. These exposure/disease pairings were excluded after the first independent Panel meeting as it was determined that they would not be appropriate for Schedule 2 and would require a gradual process injury assessment. Evidence reviews were not completed for these exposure/disease pairings because the decision to exclude them was straightforward. Included in this section are:

- Irritant and allergic dermatitis for any exposure
- Acrylonitrile and cancer
- Alcohol, glycols or ketones and diseases
- Aluminium and aluminosis, bauxite fibrosis (Shaver's disease) and chronic obstructive pulmonary disease (COPD)
- Ammonia and COPD and pulmonary fibrosis
- Antimony or its compounds and nose septal ulceration, deposits on teeth or antimoniosis
- Benzoquinone and vitiligo
- Cadmium and pulmonary emphysema, ansomia, osteoporosis, osteomalacia, itai-itai disease, nephropathy and Fanconi disease
- Carbon disulphide and chronic toxic encephalopathy, toxic optical neuropathy, ototoxic hearing loss, atherosclerosis, chronic ischaemic heart disease, secondary hypertension and chronic kidney disease
- Chlorine and COPD, emphysema, chronic bronchiolitis, pulmonary fibrosis, chronic rhinitis and erosion of the teeth
- Copper and hepatic granuloma, chronic pulmonary fibrosis and chalcosis
- Cyclophosphamide and leukaemia
- Fluorine and dental fluorosis, skeletal fluorosis and COPD
- Food flavourings and obliterative bronchiolitis
- Hard metal dust and sensitizer-induced occupational asthma and hard metal lung disease
- Isocyanates and allergic rhinitis, allergic conjunctivitis and COPD
- Lindane and non-Hodgkin's lymphoma
- Methyl ethel ketone and chronic toxic encephalopathy
- Methyl isobutyl ketone and polyneuropathy
- Mineral acids and nasal septal ulceration and laryngeal cancer
- Nail technician and respiratory diseases
- Nitroglycerin and chronic toxic encephalopathy, angina pectoris and Raynaud's phenomenon
- Non-fibrogenic mineral dust and stannosis, baritosis, pneumoconiosis due to titanium dioxide and antimoniosis

- Optical radiations and chronic blepharoconjunctivitis, chronic actinic dermatitis and actinic cataracts
- Oxides of nitrogen or its compounds and bronchiolitis obliterans, COPD and B12 deficiency
- Pentachlorophenol (PCP) and NHL
- Pesticides and anti-coagulation syndrome due to exposure to coumarin derivatives, toxic effects caused by pentachlorophenol and carcinogenic effects of pesticides
- Pharmaceutical agents and carcinogenic effects of antineoplastic drugs
- Platinum and allergic rhinitis and allergic urticaria
- Polychlorinated biphenyl and malignant melanoma
- Polycyclic aromatic hydrocarbons and lung cancer
- Selenium and selenosis
- Sulphur oxides and chronic skin and mucous membranes irritation, nose septal ulceration, COPD, chronic bronchiolitis obliterans, emphysema and pulmonary fibrosis

2.4.10 Irritant and allergic contact dermatitis

All instances of irritant and allergic contact dermatitis have been removed from consideration. Contact dermatitis is a common occupational disease, but it is complex to establish specific causation, requiring a case-by-case investigation. It is not appropriate to include dermatitis on Schedule 2.

2.4.11 Acrylonitrile or its compounds

Evidence for the Independent Panel's review	
Exposure	Acrylonitrile or its compounds
Related diseases	Cancer (not specified)
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational exposure to acrylonitrile can occur in chemical facilities where the compound is produced, in the preparation of its derived products (mainly polymers), in the manufacture of synthetic fibres and plastic materials from the polymers, and in the transformation of polymers into goods. The largest use of this bulk chemical is in the production of acrylic and modacrylic textile fibres.[1]
IARC advice	Acrylonitrile is classed as a possible carcinogen (2B) by IARC. It causes a range of tumours in animal experiments. The association between acrylonitrile exposure and lung cancer in humans is not considered strong enough to class it as a grade 1 carcinogen.[37]
NIOSH advice	Exposure routes: inhalation, skin absorption, ingestion, skin and/or eye contact. Symptoms: irritation eyes, skin; asphyxia; headache; sneezing; nausea, vomiting; lassitude (weakness, exhaustion), dizziness; skin vesiculation; scaling dermatitis; [potential occupational carcinogen].[58]
Deemed Diseases List advice	Acrylonitrile is included as an acute poisoning exposure and is linked to manufacturing.
Existing Schedule 2 entry	No relevant entry
Summary of Independent Panel's assessment	
Carcinogenic effects (2B) should be excluded now because determining causality is complex. A detailed clinical assessment is needed. This exposure/disease pairing is not suitable for Schedule 2. It is not clear if we use acrylonitrile in New Zealand, but it is possible.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.12 Alcohols, glycols, or ketones

Evidence for the Independent Panel's review	
Exposure	Alcohols, glycols, or ketones
Related disease	Diseases (not specified)
Summary statement	Insufficient causal evidence
ILO guidance notes	Alcohols, glycols, or ketones are listed as an exposure category. There are a large number of associated diseases, it would be impractical to list them all.
IARC advice	Not relevant for this exposure (not cancer).
Deemed Diseases List advice	Peripheral neuropathy and hepatitis caused by organic solvents are listed on the Deemed Diseases List.
Existing Schedule 2 entries	30: Laryngeal carcinoma diagnosed caused by sulphuric acid mists or organic solvents. 35: Chronic solvent-induced encephalopathy diagnosed caused by organic solvents, particularly styrene, toluene, xylene, trichloroethylene, methylene chloride, or white spirit. 36: Peripheral neuropathy diagnosed caused by organic solvents such as n-hexane, carbon disulphide, or trichloroethylene; pesticides such as organophosphates; acrylamide
Summary of Independent Panel's assessment	
The diseases category is broad. Methyl isobutyl ketone (MIBK) and Methyl ethyl ketone (MEK) were individually assessed. These are already covered on Schedule 2 as organic solvents against the relevant diseases.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.13 Aluminium or its compounds

Evidence for the Independent Panel's review	
Exposure	Aluminium or its compounds
Related diseases	Aluminosis, bauxite fibrosis (Shaver's disease), COPD
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational exposure to aluminium and to its compounds can occur in the mining, metallurgical and chemical industry, in the extraction of bauxite and in the preparation of aluminium, in welding, and in the production of synthetic abrasives, glass, heat-resistant materials and fibres, and commodity aluminium compounds for manufacturing uses. Powder production and aluminium welding have been associated with the highest occupational aluminium exposure.[1]
IARC advice	Not relevant for this exposure (not cancer).
Deemed Diseases List advice	Listed under other pneumoconiosis.
Existing Schedule 2 entry	No relevant entry
Summary of Independent Panel's assessment	
COPD is a consequence of potroom asthma and is therefore covered under the Independent Panel's recommendation to add potroom emissions and asthma to Schedule 2. No further evidence review is required because this is a well-established relationship. Shavers disease is excluded because it is specific to mining processes used in Western Australia and Queensland.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.14 Ammonia or its compounds

Evidence for the Independent Panel's review	
Exposure	Ammonia or its compounds
Related diseases	COPD, Pulmonary fibrosis
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational exposure occurs in the manufacture of agricultural fertilizers (ammonium nitrate and ammonium sulphate). Other bulk uses include the production of nitric acid, synthetic urea, and sodium carbonate (via the Solvay process). It is used in the manufacture of organic chemicals including acrylonitrile, caprolactam and diamines; for the production of fibre monomers, nylon, rubbers and polymer resins. It is also used in the manufacture of dyes, pesticides, plastics, explosives, pharmaceuticals and other fine chemicals. It is commonly employed in the pulp and paper, food and beverage, textile, leather, and metallurgical industries.[1]
IARC advice	Not relevant for this exposure (not cancer).
Deemed Diseases List advice	Ammonia is included under occupational asthma, with a wide range of high-risk occupations but including manufacturing, construction, and agriculture.
Existing Schedule 2 entry	No relevant entry
Summary of Independent Panel's assessment	
COPD and pulmonary fibrosis should be considered on a case-by case basis because there may be a connection (but it is not automatic) and investigation is needed if there are concerns.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.15 Antimony or its compounds

Evidence for the Independent Panel's review	
Exposure	Antimony or its compounds
Related diseases	Antimoniosis, deposits on teeth, nose septal ulceration
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational exposure to fire retardants plastics, textiles, rubber, adhesives, pigments, and paper in a mixture with halogen-containing compounds. Semiconductor manufacturing, alloy production, lead making, lead alloying, production of the condensation polymer poly-ethylene-terephthalate. Furnace workers, printing industry, limited in the preparation of medical drugs, explosives, ruby glass manufacturing, rubber manufacturing. Used in blueing steel and colouring aluminium, pewter, and zinc, and as catalysts. Used in rubber and pharmaceutical industry, petroleum industries.[1]
IARC advice	Not relevant for this exposure (not cancer).
NIOSH advice	Exposure routes: inhalation, ingestion, skin and/or eye contact. Symptoms: irritation eyes, skin, nose, throat, mouth; cough; dizziness; headache; nausea, vomiting, diarrhoea; stomach cramps; insomnia; anorexia; unable to smell properly.
Deemed Diseases List advice	Antimony is included as an acute poisoning exposure and is linked to manufacturing.
Existing Schedule 2 entry	No relevant entry
Summary of Independent Panel's assessment	
Nasal septal ulceration is caused by other activities. Antimoniosis is extremely rare. If occupational exposure was causal, all other causes of lung opacity would need to be ruled out. It would be confusing to add this to Schedule 2.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.16 Benzoquinone or its compounds

Evidence for the Independent Panel's review	
Exposure	Benzoquinone or its compounds
Related diseases	Vitiligo
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational exposure is possible in the chemical industry, where it is produced or used as a starting material, in the manufacture of hydroquinone, for fine chemicals (pharmaceuticals, pesticides, fungicides, dyes), in the rubber industry as a vulcanization accelerator, and in the textile, leather and cosmetic industries.[1]
IARC advice	Not relevant for this exposure (not cancer).
Deemed Diseases List advice	Benzoquinone is included as an acute poisoning exposure and is linked to manufacturing.
Summary of Independent Panel's assessment	
Vitiligo is best considered on a case-by-case basis as there may be many causes.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.17 Cadmium

Evidence for the Independent Panel's review	
Exposure	Cadmium
Related disease	Ansomia, Fanconi disease, Itai-itai disease, nephropathy, osteoporosis, osteomalacia, pulmonary emphysema
Summary statement	Insufficient causal evidence
ILO guidance notes	Pulmonary emphysema, ansomia, osteoporosis, osteomalacia, itai-itai disease, nephropathy and Fanconi disease caused by cadmium exposure are on the ILO List.[1]
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	Lung cancer and acute toxic poisoning caused by cadmium exposure are on the Deemed Diseases List.
Existing Schedule 2 entry	Lung cancer and chronic renal failure caused by cadmium exposure are on Schedule 2.
Summary of Independent Panel's assessment	
Pulmonary emphysema, ansomia, osteoporosis, osteomalacia and itai-itai disease are best considered on a case-by-case basis because there can be a range of causes.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.18 Carbon disulphide

Evidence for the Independent Panel's review	
Exposure	Carbon disulphide
Related disease	Chronic toxic encephalopathy, toxic optical neuropathy, ototoxic hearing loss, atherosclerosis, chronic ischaemic heart disease, secondary hypertension, chronic kidney disease
Summary statement	Insufficient causal evidence
ILO guidance notes	Chronic toxic encephalopathy, toxic optical neuropathy, ototoxic hearing loss, atherosclerosis, chronic ischaemic heart disease, secondary hypertension, chronic kidney disease, caused by carbon disulphide exposure are on the ILO List.[1]
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	Peripheral neuropathy and acute toxic poisoning caused by carbon disulphide are on the Deemed Diseases List.
Existing Schedule 2 entry	Peripheral neuropathy caused by carbon disulphide is on Schedule 2.
Summary of Independent Panel's assessment	
Chronic toxic encephalopathy, toxic optical neuropathy, ototoxic hearing loss, atherosclerosis, chronic ischaemic heart disease, secondary hypertension, and chronic kidney disease are best considered on a case-by-case basis because there can be a range of causes.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.19 Chlorine or its compounds

Evidence for the Independent Panel's review	
Exposure	Chlorine or its compounds
Related diseases	COPD, emphysema, chronic bronchiolitis, pulmonary fibrosis, chronic rhinitis, erosion of the teeth.
Summary statement	Insufficient causal evidence
ILO guidance notes (including quoted material)	Occupational exposure is possible in the chemical industry during the synthesis of derivates such as hypochlorite, hydrochloric acid, organic chlorine compounds, and calcium and zinc chloride. It is used as a bleaching agent in the textile and paper industries. Exposure may occur in water purification where chlorine is used as a disinfectant, home cleaning, and paper pulp mill work.[1]
IARC advice	Not relevant for this exposure (not cancer).
Deemed Diseases List advice	No relevant entry.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
COPD, chronic bronchiolitis, emphysema and pulmonary fibrosis, chronic rhinitis and erosion of teeth are best considered on a case-by-case basis because there can be a range of causes.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.20 Copper

Evidence for the Independent Panel's review	
Exposure	Copper
Related disease	Hepatic granuloma, chronic pulmonary fibrosis, chalcosis
Summary statement	Insufficient causal evidence
ILO guidance notes	Hepatic granuloma, chronic pulmonary fibrosis, chalcosis caused by copper exposure are on the ILO List.
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	Acute toxic poisoning caused by copper is on the Deemed Diseases List.
Existing Schedule 2 entry	Chronic renal failure caused by copper is on Schedule 2.
Summary of Independent Panel's assessment	
Linking a hepatic granuloma to copper exposure would be difficult and there is not an automatic association. Chronic pulmonary fibrosis is best considered on a case-by-case basis because there can be a range of causes. Chalcosis is an ophthalmology issue and is extremely rare.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.21 Cyclophosphamide

Evidence for the Independent Panel's review	
Exposure	Cyclophosphamide
Related disease	Leukaemia
Summary statement	Insufficient causal evidence
ILO guidance notes	Oncology nurses and pharmacists involved in preparing or administering cyclophosphamide for use with patients could be at risk of occupational exposure.[1]
Deemed Diseases List advice	No relevant entry.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
A relationship is theoretically possible in a manufacturing space but is much less likely in hospital settings due to the exposure intensity needed. This is best addressed on a case-by-case basis because of the need to assess the exposure status on an individual basis.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.22 Fluorine

Evidence for the Independent Panel's review	
Exposure	Fluorine
Related disease	Dental fluorosis, skeletal fluorosis, COPD
Summary statement	Insufficient causal evidence
ILO guidance notes	Fluorine and dental fluorosis, skeletal fluorosis and COPD are connected on the ILO List
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	Acute poisoning caused by fluorine is listed on the Deemed Diseases List.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
Dental fluorosis and skeletal fluorosis should be excluded now because we have no recent reports of this as a workplace exposure and this combination does not meet the intent of Schedule 2 (that is, it can be caused by other exposures). COPD should be excluded now because it is incidental to asthma when related to fluorine exposure.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.23 Food flavouring

Evidence for the Independent Panel's review	
Exposure	Food flavouring
Related disease	Obliterative bronchiolitis
Summary statement	Insufficient causal evidence
ILO guidance notes	Food flavouring does not appear as an exposure in the ILO List.
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	Obliterative bronchiolitis caused by food flavourings is on the Deemed Diseases List.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
This is too broad a category and this breadth is not appropriate for Schedule 2.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.24 Hard metal dust

Evidence for the Independent Panel's review	
Exposure	Hard metal dust
Related diseases	Sensitizer-induced occupational asthma, hard metal lung disease
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational exposure to hard metal dusts is possible in the production of the material, in the manufacturing of mechanical hard metal tools and in their use for drilling, sawing, cutting, polishing, or grinding operations.[1]
IARC advice	Not relevant for this exposure (not cancer).
Deemed Diseases List advice	No relevant entry on the Deemed Diseases List.
Existing Schedule 2 entry	Diseases of a type generally accepted by the medical profession caused by tungsten.
Summary of Independent Panel's assessment	
This exposure/disease pairing is likely to be sufficiently covered by existing entry 24: Diseases of a type generally accepted by the medical profession caused by tungsten.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.25 Isocyanates

Evidence for the Independent Panel's review	
Exposure	Isocyanates
Related disease	Allergic rhinitis, allergic conjunctivitis, and COPD
Summary statement	Insufficient causal evidence
ILO guidance notes	Allergic rhinitis, allergic conjunctivitis, and COPD caused by isocyanates is on the ILO List.
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	Occupational asthma caused by isocyanates is on the Deemed Diseases List.
Existing Schedule 2 entry	Occupational asthma caused by isocyanates is on Schedule 2.
Summary of Independent Panel's assessment	
Allergic rhinitis, allergic conjunctivitis, and COPD would need to be considered on a case-by-case basis and are not suitable for Schedule 2 because there can be a range of causes.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.26 Lindane

Evidence for the Independent Panel's review	
Exposure	Lindane
Related disease	Non-Hodgkin's lymphoma (NHL)
Summary statement	Insufficient causal evidence
ILO guidance notes	ILO has not linked lindane exposure and NHL.
IARC advice	There is sufficient evidence to link lindane and NHL.[37]
Deemed Diseases List advice	NHL caused by lindane is listed on the Deemed Diseases List.
Existing Schedule 2 entry	No relevant entry
Summary of Independent Panel's assessment	
Lindane is a pesticide banned for use in Aotearoa New Zealand in 2009. Any exposure cases or NHL would be historical. Pesticides is a broad category and is too vague. Dioxins are the contaminants of interest and carcinogenic effects are already covered. It may be best considered on a case-by-case basis.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.27 Methyl ethyl ketone and chronic toxic encephalopathy

Evidence for the Independent Panel's review	
Exposure	Methyl ethyl ketone (MEK), also known as 2-butanone
Related diseases	Chronic toxic encephalopathy
Summary statement	Insufficient causal evidence
ILO guidance notes	Methyl ethyl ketone is absorbed by inhalation and from the skin, where it causes mild irritation and produces dermatitis by removal of skin lipids. It is a mild narcotic. There is a report of retrobulbar neuritis in a young worker exposed to this solvent. MEK is also an oxidation biotransformation product of 2-butanol. The ILO has not connected chronic toxic encephalopathy (CTE) to MEK; however, CTE is connected to alcohols, and MEK is connected to acute toxic encephalopathy.[1]
IARC advice	Not relevant for this exposure (not cancer).
NIOSH advice	Many classes of chemicals are used as organic solvents, including aliphatic hydrocarbons, aromatic hydrocarbons, amines, esters, ethers, ketones, and nitrated or chlorinated hydrocarbons.
UK Health Security Agency advice	Chronic exposure to low levels of MEK results in neurological effects. Two cases of MEK exposure that lead to encephalopathy are presented – one chronic, one acute.[59]
Deemed Diseases List advice	Acute poisoning caused by ketones is listed on the Deemed Diseases List.
Existing Schedule 2 entry	This may be covered in entry 35: Chronic solvent-induced encephalopathy diagnosed caused by organic solvents, particularly styrene, toluene, xylene, trichloroethylene, methylene chloride, or white spirit.
Summary of Independent Panel's assessment	
This exposure/disease pairing is covered on Schedule 2 by entry 35 (referenced above).	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.28 Methyl isobutyl ketone and polyneuropathy

Evidence for the Independent Panel's review	
Exposure	Methyl isobutyl ketone (MIBK)
Related diseases	Polyneuropathy
Summary statement	Insufficient causal evidence
ILO guidance notes	Exposure to MIBK may lead, similarly to exposure to *n*-hexane, to polyneuropathy due to the neurotoxic activity of the main metabolite of both substances, 2,5-hexanedione. For this common aetiology, the clinical and histopathological pictures are similar.[1]
IARC advice	Not applicable for this disease (not cancer).
Deemed Diseases List advice	Peripheral neuropathy diagnosed caused by organic solvents is listed on the Deemed Diseases List.
Existing Schedule 2 entry	This exposure/disease pairing is potentially covered by entry 36: Peripheral neuropathy diagnosed caused by organic solvents such as n-hexane, carbon disulphide, or trichloroethylene; pesticides such as organophosphates; acrylamide.
Summary of Independent Panel's assessment	
This exposure/disease pairing is covered on Schedule 2 by entry 36 (referenced above).	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.29 Mineral acids

Evidence for the Independent Panel's review	
Exposure	Mineral acids
Related disease	Nasal septal ulceration, laryngeal cancer
Summary statement	Insufficient causal evidence
ILO guidance notes	Erosion and ulceration of the mucosal membrane or perforation of the nasal septum have been described in subjects chronically exposed to gas or mist of hydrogen chloride or sulphuric acid. Mists from strong inorganic acids (eg, sulphuric, hydrochloric, nitric, and phosphoric acids) have been classified as Group 1 carcinogens (i.e., carcinogenic to humans) by IARC because of the increased risk of laryngeal cancer in occupationally exposed workers. The highest risk levels have been observed in association with pickling operations (i.e., removal of scale and oxides from the metal surface) within the steel industry.[1]
IARC advice	Laryngeal cancer caused by strong inorganic acid mists is listed as having sufficient evidence for causality in humans.[37] Mineral acids or mists not mentioned.
Deemed Diseases List advice	Acute poisoning or toxicity caused by mineral acids is on the Deemed Diseases List.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
Nasal septal ulceration is caused by other activities. Smoking as a causal factor cannot be excluded for laryngeal cancer (and smoking is the main cause).	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.30 Nail technician

Evidence for the Independent Panel's review	
Exposure	Nail technician (working in a nail salon)
Related disease	Respiratory diseases
Summary statement	Insufficient causal evidence
ILO guidance notes	No relevant entry.
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	No relevant entry.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
Respiratory disease is too broad a category. We conducted a board search for evidence for this disease/exposure pairing, there was some low-quality evidence from the 1990's and early 200's but nothing substantive and nothing recent.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.31 Nitroglycerin and nitric acid esters

Evidence for the Independent Panel's review	
Exposure	Nitroglycerin and nitric acid esters
Related diseases	Chronic toxic encephalopathy, angina pectoris, Raynaud's phenomenon
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational exposure to nitroglycerin and nitric acid esters occurs in mining, demolition, military and pharmaceuticals. Most nitro-esters are employed as explosives both for civil purposes (mining, earthwork and demolition) and in the military as propellants for projectiles and rockets and as blast agents. Small quantities are used in the pharmaceutical industry. Nitroglycerine is highly explosive and still used by itself for this purpose in certain applications (eg, in oil-well drilling). More often, it is used with EGDN to make dynamite or with guncotton to make cordite or other smokeless powders and in rocket propellants.[1]
IARC advice	Not relevant to this exposure.
NIOSH advice	Exposure routes include inhalation, skin absorption, ingestion, skin and/or eye contact. Symptoms include throbbing headache; dizziness; nausea, vomiting, abdominal pain; hypotension; flush; palpitations; methemoglobinemia; delirium, central nervous system depression; angina; skin irritation.[60]
Deemed Diseases List advice	Nitroglycerin (or other nitric acid esters); is listed as an acute poisoning exposure and is linked to manufacturing.
Summary of Independent Panel's assessment	
Nitroglycerine is not approved for use in Aotearoa New Zealand.[61] Raynaud's phenomenon is impossible to assess in relation to occupation.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.32 Non-fibrogenic mineral dust

Evidence for the Independent Panel's review	
Exposure	Non-fibrogenic mineral dust
Related diseases	Stannosis, baritosis, pneumoconiosis due to titanium dioxide, Antimoniosis
Summary statement	Insufficient causal evidence
ILO guidance notes	Non-fibrogenic mineral dust exposure occurs in occupations involving mining, smelting, refining, and production processes of tin. The mining, grinding and bagging of barite, and in the production and packaging of raw material (rutile) and in the manufacture of paints and paper that contain it as a white pigment.[1]
IARC advice	Not relevant for this exposure (not cancer).
Deemed Diseases List advice	No relevant entry.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
Titanium dioxide is used in sunscreen and some paints. There is insufficient evidence to determine causality between the exposure/disease pairing. Other dusts are already covered in Schedule 2 (items 26, 28, 37 and 38). Baritosis is best considered on a case-by-case basis because there can be other causes. Antimoniosis is extremely rare. If antimoniosis was an occupational disease, all other causes of lung opacity would need to be ruled out. This means that a detailed clinical assessment and work history assessment would be required.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.33 Optical radiation

Evidence for the Independent Panel's review	
Exposure	Optical radiation
Related disease	Chronic blepharoconjunctivitis, chronic actinic dermatitis, actinic cataract
Summary statement	Insufficient causal evidence
ILO guidance notes	Chronic blepharoconjunctivitis, chronic actinic dermatitis, actinic cataract caused by optical radiation are on the ILO List.
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	No relevant entry.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
Chronic blepharoconjunctivitis, chronic actinic dermatitis, actinic cataract caused by UV, malignant melanoma and non-melanoma skin cancers would need to be evaluated on a case-by-case basis.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.34 Oxides of nitrogen

Evidence for the Independent Panel's review	
Exposure	Oxides of nitrogen
Related diseases	Bronchiolitis obliterans, COPD, B12 deficiency
Summary statement	Insufficient causal evidence
ILO guidance notes	Nitrogen oxides are released from the exhaust of motor vehicles, the burning of coal, oil, or natural gas, and during arc welding, electroplating, engraving, and dynamite blasting, the manufacturing of civil explosives, rocket fuels, and military ordnance. Fumes of nitrogen oxides are generated in fires in the low-temperature aging of nitrate-containing materials, such as fertilizers (ammonium nitrate) and aged ammunition.[1]
IARC advice	Advice not relevant for occupational exposures (air pollution covered by IARC).
Deemed Diseases List advice	Oxides of nitrogen are included as an acute poisoning exposure and is linked to manufacturing.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
Nitrogen oxides are occupational irritants, with transient and acute effects. Acute effect is not appropriate for Schedule 2. Adverse respiratory health effects from this exposure require extremely high exposures. Such instances are better dealt with on a case-by-case basis. B12 deficiency is specific and transient.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.35 Pentachlorophenol (PCP)

Evidence for the Independent Panel's review	
Exposure	PCP
Related disease	Non-Hodgkin's lymphoma (NHL)
Summary statement	Insufficient causal evidence
ILO guidance notes	'Toxic effects' of PCP is listed under the section relating to pesticide in the ILO List.
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	NHL caused by PCP is listed on the Deemed Diseases List, but it notes that exposure is uncommon in Australia although it could still occur through treatment of some wood products.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
Any exposure or NHL would be historical. Pesticides is a broad category and is too vague. Dioxins are the contaminants of interest and carcinogenic effects are already covered. It may be best considered on a case-by-case basis.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.36 Pesticides

Evidence for the Independent Panel's review	
Exposure	Pesticides
Related disease	Anti-coagulation syndrome due to exposure to coumarin derivatives, toxic effects caused by pentachlorophenol, and carcinogenic effects of pesticides.
Summary statement	Insufficient causal evidence
ILO guidance notes	Anti-coagulation syndrome due to exposure to coumarin derivatives, toxic effects caused by pentachlorophenol, and carcinogenic effects of pesticides caused by pesticides are on the ILO List.[1]
IARC advice	Not relevant for these diseases (not cancer).
Deemed Diseases List advice	Occupational asthma, acute toxic poisoning and peripheral neuropathy caused by pesticides is on the Deemed Diseases List.
Existing Schedule 2 entry	Peripheral neuropathy caused by pesticides is on Schedule 2.
Summary of Independent Panel's assessment	
Pesticides is a broad category and is too vague. Dioxins are the contaminants of interest for PCP and carcinogenic effects are already covered (referenced above).	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.37 Pharmaceutical agents

Evidence for the Independent Panel's review	
Exposure	Pharmaceutical agents
Related disease	Carcinogenic effects of antineoplastic drugs
Summary statement	Insufficient causal evidence
ILO guidance notes	Several antineoplastic agents have carcinogenic properties (to the point that the International Agency for Research on Cancer classified some as Group 1 carcinogens), but there is no firm epidemiological evidence of an increased cancer risk in exposed workers. Working in an oncology pharmacy or ward might theoretically entail prolonged exposures over time; as such, according to the precautionary principle, all preventive measures (see below) must always be implemented.[1]
IARC advice	Cyclophosphamide, Etoposide (in combination with cisplatin and bleomycin) are chemotherapy drugs that IARC states as having sufficient evidence of carcinogenic effects on humans; however, this was not specific to occupational exposure. Secondary carcinogenic impacts of these drugs are a greater risk to cancer patients receiving these drugs.[37]
Deemed Diseases List advice	Bladder cancer and leukaemia caused by cyclophosphamide is on the Deemed Diseases List.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
This appears to relate to carcinogenic anti-neoplastics. A relationship is theoretically possible in a manufacturing space but is much less likely in hospital settings due to the exposure intensity needed. This is best addressed on a case-by-case basis.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.38 Platinum or its compounds

Evidence for the Independent Panel's review	
Exposure	Platinum or its compounds
Related disease	Allergic rhinitis and allergic urticaria
Summary statement	Insufficient causal evidence
ILO guidance notes	Occupational exposure to platinum or its compounds can occur in the following sectors and jobs: platinum mining facilities and refineries, catalyst manufacturers and recyclers, jewellers, chemical and electronic manufacturers, the pharmaceutical industry, hospitals and healthcare facilities, and dental offices.[1]
IARC advice	Not relevant for this exposure (not cancer).
Deemed Diseases List advice	No relevant entry.
Existing Schedule 2 entry	No relevant entry.
Summary of Independent Panel's assessment	
Platinum is a known irritant but due to the various uses and occupations involved in platinum exposure, it is best assessed on a case-by-case basis.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.39 Polychlorinated biphenyls and malignant melanoma

Evidence for the Independent Panel's review	
Exposure	Polychlorinated biphenyls (PCBs)
Related diseases	Melanoma
Summary statement	Insufficient causal evidence
ILO guidance notes	The ILO notes that exposure to PCBs is uncommon. Exposure can occur by coming into contact with electrical fittings (industrial electricians, electrical power line and cable workers, electrical mechanics, and electricians), in the disposal of electrical material (waste storage, incineration and contaminated site remediation), in welding and during general maintenance workers. Fire-fighters may also be exposed.
IARC advice	PCBs are listed as potential carcinogens for breast cancer and non-Hodgkin's lymphoma.[37]
Deemed Diseases List advice	Melanoma caused by PCBs is listed on the Deemed Diseases List.
Existing Schedule 2 entry	Primary epitheliomatous cancer of the skin diagnosed as caused by tar, pitch, bitumen, mineral oil, anthracene, or the compounds, products, or residues of these substances.
Summary of Independent Panel's assessment	
PCBs are banned in Aotearoa New Zealand. While exposure (historic or illegal) is possible, it would require a case-by-case assessment and thus not appropriate for Schedule 2.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.40 Polycyclic aromatic hydrocarbons and lung cancer

Evidence for the Independent Panel's review	
Exposure	Polycyclic aromatic hydrocarbons (PAHs)
Related diseases	Lung cancer
Summary statement	Insufficient causal evidence
ILO guidance notes	Impractical to list as PAHs are referenced in several exposure categories.
IARC	Limited evidence of carcinogenicity in humans – more research required.[37]
Deemed Diseases List advice	PAHs are listed as an exposure linked to lung cancer on the Deemed Diseases List.
Existing Schedule 2 entry	Lung cancer diagnosed caused by bis (chloromethyl) ether (and chloromethyl methyl ether), cadmium, coke oven emissions, nickel, radon, silica, or soot.
Summary of Independent Panel's assessment	
PAHs sufficiently covered by the current Schedule 2 entry soots and coke-oven emissions (of which PAHs are relevant agents).	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.41 Selenium or its compounds

Evidence for the Independent Panel's review	
Exposure	Selenium or its compounds
Related diseases	Selenosis
Summary statement	Insufficient causal evidence
ILO guidance notes (including quoted material)	The largest industrial use of elemental selenium and of its compounds is in glass manufacturing, in deep red to light orange pigments for paints, plastics, ceramics, and glazes and as a chemical reagent for the preparation of specialty chemicals. Its use in electrical and electronic devices is declining, but it is used in plain paper photocopiers and laser printers, as well as in photovoltaic (solar) cells.[1]
IARC advice	Not relevant for this exposure (not cancer).
NIOSH advice	Exposure routes: inhalation, ingestion, skin and/or eye contact. Symptoms: irritation eyes, skin, nose, throat; visual disturbance; headache; chills, fever; dyspnea (breathing difficulty), bronchitis; metallic taste, garlic breath, gastrointestinal disturbance; dermatitis; eye, skin burns; In Animals: anaemia; liver necrosis, cirrhosis; kidney, spleen damage.[62]
Deemed Diseases List advice	Selenium is included as an acute poisoning exposure and is linked to manufacturing.
Existing Schedule 2 entry	No relevant entry
Summary of Independent Panel's assessment	
Selenosis is best considered on a case-by-case basis.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

2.4.42 Sulphur or its compounds

Evidence for the Independent Panel's review	
Exposure	Sulphur or its compounds
Related diseases	Chronic skin and mucous membranes irritation, nose septal ulceration, COPD, chronic bronchiolitis obliterans, emphysema, pulmonary fibrosis.
Summary statement	Insufficient causal evidence
ILO guidance notes	Current industrial uses of sulphur dioxide are mainly in rubber vulcanization, while its use as a refrigerant fluid in industrial cooling units has been largely superseded by other chemical compounds. Sulphur dioxide is an authorized food preserving agent and is added (eg, to wine) either as such, bubbling gas from a cylinder, or as solid sodium metabisulphite salt. Occupational exposure to sulphur trioxide typically occurs in the chemical industry, in the manufacture of sulphuric acid and oleum, and in chemical processes such as the sulphonation of organic acids with sulphur trioxide.[1]
IARC advice	Not relevant to this exposure (not cancer).
Deemed Diseases List advice	Laryngeal cancer diagnosed caused by sulphuric acid mists.
Existing Schedule 2 entry	Laryngeal carcinoma diagnosed caused by sulphuric acid mists or organic solvents.
Summary of Independent Panel's assessment	
Nasal septal ulceration is caused by other activities. Chronic skin and mucous membrane irritation, COPD, chronic bronchiolitis obliterans, emphysema and pulmonary fibrosis are best considered on a case-by-case basis because there are many causes of these diseases.	
Independent Panel recommendation	**Do not recommend inclusion on Schedule 2**

Appendix A: References

1. International Labour Organization. Diagnostic and exposure criteria for occupational diseases [Internet]. 2022. Available from: https://www.ilo.org/global/topics/safety-and-health-at-work/resources-library/publications/WCMS_836362

2. Driscoll T. Deemed diseases in Australia. Canberra: SafeWork Australia; 2021.

3. Ministry of Business, Innovation and Employment. Summary of Submissions – Seeking Proposals for Additions to the Schedule 2 List of Occupational Diseases under the Accident Compensation Act 2001. 2023; Available from: https://www.mbie.govt.nz/dmsdocument/26880-summary-of-submissions-to-schedule-2-pdf

4. Driscoll TR. Deemed diseases revised list and guidance. 2021.

5. National Institute for Occupational Safety and Health. Ammonia [Internet]. 2019 [cited 2023 Nov 2]. Available from: https://www.cdc.gov/niosh/topics/ammonia/default.html

6. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Ammonia [Internet]. 2019 [cited 2023 Nov 2]. Available from: https://www.cdc.gov/niosh/npg/npgd0028.html

7. International Agency for Research on Cancer, editor. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 100C. Lyon: International agency for research on cancer; 2012. (IARC monographs on the evaluation of carcinogenic risks to humans).

8. Reid G, Klebe S, van Zandwijk N, George AM. Asbestos and Zeolites: from A to Z via a Common Ion. Chem Res Toxicol. 2021;34:936–51.

9. National Institute for Occupational Safety and Health, Smith, Moss, Brown. Health Hazard Evaluation Report HETA 98–0224–2714. 1998;

10. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Nickel metal and other compounds (as Ni) [Internet]. 2019 [cited 2023 Oct 31]. Available from: https://www.cdc.gov/niosh/npg/npgd0445.html

11. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Fluorine [Internet]. 2019 [cited 2023 Nov 1]. Available from: https://www.cdc.gov/niosh/npg/npgd0289.html

12. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 100D [Internet]. 2012. Available from: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Radiation-2012

13. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 110 [Internet]. 2014. Available from: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Some-Chemicals-Used-As-Solvents-And-In-Polymer-Manufacture-2016

14. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Propylene dichloride [Internet]. 2019 [cited 2023 Nov 2]. Available from: https://www.cdc.gov/niosh/npg/npgd0534.html

15. Seeherunwong A, Chaiear N, Khuntikeo N, Ekpanyaskul C. Cholangiocarcinoma Attributed to Occupation: A Systematic Reviews. Asian Pac J Cancer Prev. 2022;23:1837–45.

16. National Institute for Occupational Safety and Health. Asbestos [Internet]. 2023 [cited 2023 Oct 27]. Available from: https://www.cdc.gov/niosh/topics/asbestos/default.html

17. Institute of Medicine. Asbestos: Selected Cancers [Internet]. Washington, D.C.: National Academies Press; 2023 [cited 2023 Oct 27]. Available from: http://www.nap.edu/catalog/11665

18. Camargo MC, Stayner LT, Straif K, Reina M, Al-Alem U, Demers PA, et al. Occupational Exposure to Asbestos and Ovarian Cancer: A Meta-analysis. Environ Health Perspect. 2011;119:1211–7.

19. Reid A, De Klerk N, Musk AW (Bill). Does Exposure to Asbestos Cause Ovarian Cancer? A Systematic Literature Review and Meta-analysis. Cancer Epidemiol Biomarkers Prev. 2011;20:1287–95.

20. Slomovitz B, De Haydu C, Taub M, Coleman RL, Monk BJ. Asbestos and ovarian cancer: examining the historical evidence. Int J Gynecol Cancer. 2021;31:122–8.

21. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 97 [Internet]. 2008. Available from: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/1-3-Butadiene-Ethylene-Oxide-And-Vinyl-Halides-Vinyl-Fluoride-Vinyl-Chloride-And-Vinyl-Bromide--2008

22. National Institute for Occupational Safety and Health. 1,3-butadiene. 1984 [cited 2023 Oct 27]; Available from: https://www.cdc.gov/niosh/docs/84-105/default.html

23. Occupational Safety and Health Administration. 1,3-Butadiene - Health Effects [Internet]. [cited 2023 Oct 27]. Available from: https://www.osha.gov/butadiene/health-effects

24. Sathiakumar N, Bolaji BE, Brill I, Chen L, Tipre M, Leader M, et al. 1,3-Butadiene, styrene and lymphohaematopoietic cancers among North American synthetic rubber polymer workers: exposure–response analyses. Occup Environ Med. 2021;78:859–68.

25. Demers PA, DeMarini DM, Fent KW, Glass DC, Hansen J, Adetona O, et al. Carcinogenicity of occupational exposure as a firefighter (IARC). Lancet Oncol. 2022;23:985–6.

26. National Institute for Occupational Safety and Health. Firefighter Cancer Awareness [Internet]. 2021 [cited 2023 Oct 30]. Available from: https://www.cdc.gov/niosh/newsroom/feature/firefighter-cancer-awareness.html

27. Casjens S, Brüning T, Taeger D. Cancer risks of firefighters: a systematic review and meta-analysis of secular trends and region-specific differences. Int Arch Occup Environ Health. 2020;93:839–52.

28. Soteriades ES, Kim J, Christophi CA, Kales SN. Cancer Incidence and Mortality in Firefighters: A State-of-the-Art Review and Meta-Analysis. Asian Pac J Cancer Prev APJCP. 2019;20:3221–31.

29. Jalilian H, Ziaei M, Weiderpass E, Rueegg CS, Khosravi Y, Kjaerheim K. Cancer incidence and mortality among firefighters. Int J Cancer. 2019;145:2639–46.

30. Laroche E, L'Espérance S. Cancer Incidence and Mortality among Firefighters: An Overview of Epidemiologic Systematic Reviews. Int J Environ Res Public Health. 2021;18:2519.

31. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 106. 2014.

32. Centre for Diseases Control. Trichloroethylene (TCE) | Public Health Statement [Internet]. 2020 [cited 2023 Oct 27]. Available from: https://wwwn.cdc.gov/TSP/PHS/PHS.aspx?phsid=171&toxid=30

33. Karami S, Lan Q, Rothman N, Stewart PA, Lee KM, Vermeulen R, et al. Occupational trichloroethylene exposure and kidney cancer risk: a meta-analysis. Occup Environ Med. 2012;69:858–67.

34. Scott CS, Jinot J. Trichloroethylene and cancer: systematic and quantitative review of epidemiologic evidence for identifying hazards. Int J Environ Res Public Health. 2011;8:4238–72.

35. Fedeli U, Girardi P, Mastrangelo G. Occupational exposure to vinyl chloride and liver diseases. World J Gastroenterol. 2019;25:4885–91.

36. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 58. 1993.

37. International Agency for Research on Cancer. List of classifications by cancer sites with sufficient or limited evidence in humans, IARC Monographs Volumes 1–134a [Internet]. 2023. Available from: https://monographs.iarc.who.int/wp-content/uploads/2019/07/Classifications_by_cancer_site.pdf

38. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Cadmium dust [Internet]. 2019 [cited 2023 Oct 27]. Available from: https://www.cdc.gov/niosh/npg/npgd0087.html

39. Song J kun, Luo H, Yin X hai, Huang G lei, Luo S yang, Lin D ren, et al. Association between cadmium exposure and renal cancer risk: a meta-analysis of observational studies. Sci Rep. 2015;5:17976.

40. International Agency for Research on Cancer. Coal-Tar Pitch. In: Chemical Agents and Related Occupations [Internet]. International Agency for Research on Cancer; 2012 [cited 2023 Oct 26]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK304423/

41. US Department of Health and Human Services. 15th Report on Carcinogens [Internet]. National Toxicology Program. 2021 [cited 2023 Nov 3]. Available from: https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc

42. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 100F [Internet]. 2012 [cited 2023 Oct 30].

Available from: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Chemical-Agents-And-Related-Occupations-2012

43. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Formaldehyde [Internet]. 2019 [cited 2023 Oct 30]. Available from: https://www.cdc.gov/niosh/npg/npgd0293.html

44. La Torre G, Vitello T, Cocchiara RA, Della Rocca C. Relationship between formaldehyde exposure, respiratory irritant effects and cancers: a review of reviews. Public Health. 2023;218:186–96.

45. Allegra A, Spatari G, Mattioli S, Curti S, Innao V, Ettari R, et al. Formaldehyde Exposure and Acute Myeloid Leukemia: A Review of the Literature. Med Kaunas Lith. 2019;55:638.

46. Mundt KA, Gallagher AE, Dell LD, Natelson EA, Boffetta P, Gentry PR. Does occupational exposure to formaldehyde cause hematotoxicity and leukemia-specific chromosome changes in cultured myeloid progenitor cells? Crit Rev Toxicol. 2017;47:592–602.

47. Zhang L, Tang X, Rothman N, Vermeulen R, Ji Z, Shen M, et al. Occupational exposure to formaldehyde, hematotoxicity, and leukemia-specific chromosome changes in cultured myeloid progenitor cells. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2010;19:80–8.

48. Gates A, Jakubowski JA, Regina AC. Nickel Toxicology. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Oct 24]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK592400/

49. Kolberg L, Forster F, Gerlich J, Weinmayr G, Genuneit J, Windstetter D, et al. Nickel allergy is associated with wheezing and asthma in a cohort of young German adults: results from the SOLAR study. ERJ Open Res. 2020;6:00178–2019.

50. Brera S, Nicolini A. Respiratory manifestations due to nickel. Acta Otorhinolaryngol Ital. 2005;25:113–5.

51. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Platinum [Internet]. 2019 [cited 2023 Oct 26]. Available from: https://www.cdc.gov/niosh/npg/npgd0519.html

52. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 92 [Internet]. 2010. Available from: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Some-Non-heterocyclic-Polycyclic-Aromatic-Hydrocarbons-And-Some-Related-Exposures-2010

53. CDC. Polycyclic Aromatic Hydrocarbons (PAHs) | Public Health Statement | ATSDR [Internet]. 1995 [cited 2023 Nov 3]. Available from: https://wwwn.cdc.gov/TSP/PHS/PHS.aspx?phsid=120&toxid=25

54. Rahman HH, Toohey W, Munson-McGee SH. Exposure to arsenic, polycyclic aromatic hydrocarbons, metals, and association with skin cancers in the US adults. Environ Sci Pollut Res. 2023;30:101681–708.

55. Weistenhöfer W, Lutz R, Hiller J, Schmitz-Spanke S, Drexler H. Syncarcinogenesis of natural UV radiation and polycyclic aromatic hydrocarbons in the development of squamous cell carcinomas of the skin? J Dtsch Dermatol Ges J Ger Soc Dermatol JDDG. 2022;20:1179–86.

56. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Thallium [Internet]. 2019 [cited 2023 Nov 2]. Available from: https://www.cdc.gov/niosh/npg/npgd0608.html

57. National Institute for Occupational Safety and Health. Pocket Guide to Chemical Hazards - Vanadium dust [Internet]. 2019 [cited 2023 Oct 26]. Available from: https://www.cdc.gov/niosh/npg/npgd0653.html

58. National Institute for Occupational Safety and Health. CDC - NIOSH Pocket Guide to Chemical Hazards - Acrylonitrile [Internet]. [cited 2023 Nov 29]. Available from: https://www.cdc.gov/niosh/npg/npgd0014.html

59. United Kingdom Health Security Agency. Methyl ethyl ketone: toxicological overview [Internet]. 2021. Available from: https://www.gov.uk/government/publications/methyl-ethyl-ketone-properties-and-incident-management/methyl-ethyl-ketone-toxicological-overview

60. National Institute for Occupational Safety and Health. CDC - NIOSH Pocket Guide to Chemical Hazards - Nitroglycerine [Internet]. [cited 2023 Nov 29]. Available from: https://www.cdc.gov/niosh/npg/npgd0456.html

61. Worksafe. Workplace exposure standards and biological exposure indices [Internet]. 2022. Available from: https://www.worksafe.govt.nz/dmsdocument/20238-workplace-exposure-standards-and-biological-exposure-indices-edition-13/latest

62. National Institute for Occupational Safety and Health. CDC - NIOSH Pocket Guide to Chemical Hazards - Selenium [Internet]. [cited 2023 Nov 29]. Available from: https://www.cdc.gov/niosh/npg/npgd0550.html

Appendix B: Abbreviations list

95% CI	95% confidence interval (i.e., a 5% chance of being incorrect)
AC Act	Accident Compensation Act 2001
ACC	Accident Compensation Corporation
C	Cohort study
CC	Case-control study
CCA	Cholangiocarcinoma
CDC	Centres for Diseases Control
COPD	Chronic obtrusive pulmonary disease
DCM	Dichloromethane
DD	Deemed Diseases
ILO	International Labour Organisation
IARC	International Agency for Cancer Research
IOM	Institute of Medicine
MBIE	Ministry of Business, Innovation and Employment
MEK	Methyl ethyl ketone
MIBK	Methyl isobutyl ketone
MSIR	Meta standard incidence ratio
MSMR	Meta standard mortality ratio
NIOSH	National Institute of Occupational Safety and Health
NHL	Non-Hodgkin's lymphoma
OR	Odds ratio
PCP	Pentachlorophenol
PICO(T/S)	Acronym for framework to strengthen evidence gathering: population, intervention, comparator, outcome, timing, setting
Ppm	Parts per million
RCT	Randomised control-trial
RR	Relative risk
SIR	Standard incidence ratio
SIRE	Standard incidence risk estimate
SMR	Standard mortality ratio
SMRE	Standard mortality ratio estimate

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