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# The NIOSH Occupational Exposure Banding Process: Guidance for the Evaluation of Chemical Hazards

External Review Draft

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention  
National Institute for Occupational Safety and Health

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# 1 Executive Summary

2 Occupational Exposure Limits (OELs) play a critical role in protecting workers and emergency response  
3 personnel from exposure to dangerous concentrations of hazardous materials [Cook 1987; Schulte et al.  
4 2010; Nikfar and Malekirad 2014; Deveau et al. 2015; Skowroń and Czerczak 2015]. In the absence of  
5 an OEL, determining the appropriate controls needed to protect workers from chemical exposures can be  
6 challenging. According to the Environmental Protection Agency (EPA), the Toxic Substances Control  
7 Act (TSCA) Chemical Substance Inventory currently contains over 85,000 chemicals that are  
8 commercially available [EPA 2015] yet only about 1,000 of these chemicals have been assigned an  
9 authoritative (government, consensus, or peer reviewed) OEL. Furthermore, the rate at which new  
10 chemicals are being introduced into commerce significantly outpaces OEL development, creating a need  
11 for guidance on thousands of chemicals that lack reliable exposure limits [Michaels 2014]. Occupational  
12 exposure banding, also known as hazard banding or health hazard banding, is a systematic process that  
13 uses both qualitative and quantitative hazard information on selected health effect endpoints to identify  
14 potential exposure ranges or categories. **The NIOSH occupational exposure banding process seeks to  
15 create a consistent and documented process to characterize chemical hazards so timely and well-  
16 informed risk management decisions can be made for chemicals lacking OELs.**

17 The concept of using hazard-based categories to communicate potential health concerns, signal workers  
18 and employers to the need for risk management, and inform exposure control requirements is not new.  
19 Numerous hazard classification and category-based systems have seen extensive use in the occupational  
20 setting. Such systems are deeply embedded in occupational hygiene practice, particularly in the  
21 pharmaceutical industry [Naumann et al. 1996; NIOSH 2009c], and are also elements of well-developed,  
22 modern hazard communication programs (e.g., United Nations 2013 Globally Harmonized System of  
23 Classification and Labelling of Chemicals). The NIOSH occupational exposure banding process is  
24 distinguished from other hazard classification and category-based systems in several ways. The unique  
25 attributes of the NIOSH process include (1) a three-tiered system that allows users of varying expertise  
26 to utilize the process, (2) determination of potential health impacts based on nine toxicological endpoints  
27 separately, (3) hazard-based categories linked to quantitative exposure ranges, and (4) assessment of the  
28 process via extensive evaluation exercises to determine accuracy and repeatability.

29 Each tier of the process has different requirements for data sufficiency, which allows a variety of  
30 stakeholders to use the process in many different situations. The most appropriate tier for banding  
31 depends on the availability and quality of the data, how it will be used, and the training and expertise of  
32 the user. While Tier 1 requires relatively little information and modest specialized training, each  
33 successive tier requires more chemical-specific data and more user expertise to successfully assign an  
34 occupational exposure band (OEB). A primary goal of Tier 1 is to give the user a quick summary of the  
35 most important health effects associated with exposure to the chemical of interest and to quickly identify  
36 toxic chemicals that should be considered for substitution or elimination. Tier 1 would likely be most be  
37 appropriate when banding a large amount of chemicals and deciding which ones should be prioritized

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1 for elimination or substitution. In general, Tier 1 can be used as a quick screening method, but NIOSH  
2 recommends going to Tier 2 if the user expertise and data are available. It should be noted that if the  
3 Tier 1 evaluation results in a band E, Tier 2 is optional given that band E represents the lowest exposure  
4 concentration range and a Tier 2 process would not result in a more stringent recommendation.  
5 However, completing the Tier 2 process could be beneficial even in this situation, as the user may gather  
6 more detailed chemical information and possibly move the chemical into a different band. Tier 2  
7 requires the user to examine a number of publicly available databases and extract relevant toxicological  
8 and weight-of-evidence data to be used in the NIOSH banding algorithm. Tier 3 employs a critical  
9 assessment to evaluate experimental data and discern toxicological outcomes.

10 The NIOSH occupational exposure banding process considers the health effects associated with nine  
11 standard toxicological health endpoints. Endpoints evaluated include acute toxicity, skin corrosion and  
12 irritation, serious eye damage and irritation, respiratory sensitization, skin sensitization, genotoxicity,  
13 carcinogenicity, reproductive/developmental toxicity, and specific target organ toxicity resulting from  
14 repeated exposure. The process looks at each health endpoint separately for each chemical, and the  
15 endpoint bands allow the user to make judgements about which health effects are the primary concern  
16 for workers who are exposed. This type of specificity allows users to customize their control strategies  
17 based on both the potency of the chemical and the target organ/health effect. In Tier 1, respiratory and  
18 skin sensitization are considered together as one endpoint due to the construction of the H-codes, which  
19 are alphanumeric codes used in the Globally Harmonized System of Classification and Labelling of  
20 Chemicals (GHS) to designate hazards.

21 Another important component of the NIOSH occupational exposure banding process is the five exposure  
22 bands. Occupational exposure banding uses limited chemical toxicity data to group chemicals into one  
23 of five bands ranging from A through E. These bands, or OEBs, define the range of exposures expected  
24 to protect worker health. Band E represents the lowest exposure concentration range recommendation,  
25 while band A represents the highest exposure concentration range [McKernan et al. 2016]. Users should  
26 note that throughout this document, bands that represent lower exposure ranges are referred to as more  
27 “protective” than bands that represent higher exposure ranges.

28  
29 The occupational exposure banding process can be used to identify potential health effects and target  
30 organs, identify health risks that impact health communication, inform decisions regarding control  
31 interventions, inform medical surveillance decisions, and provide critical information quickly. One  
32 major benefit of occupational exposure banding is that the amount of time and data required to  
33 categorize a chemical into an OEB is far less than that required to develop an OEL. However, there is  
34 greater uncertainty as to whether the OEB is as protective as an OEL produced by a rigorous risk  
35 assessment process. **An OEB is not meant to replace an OEL, rather it serves as a starting point to**  
36 **inform risk management decisions.** An OEB can also assist with prioritization of chemicals for which  
37 an OEL should be developed.

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1 NIOSH has performed evaluation exercises to ensure the accuracy and repeatability of the occupational  
2 exposure banding process. To evaluate the Tier 1 process, NIOSH compared the OELs of 600 chemicals  
3 to the Tier 1 band for those chemicals. This evaluation found that the NIOSH Tier 1 banding process  
4 resulted in a band that included the OEL or was more protective than the OEL for 91.5% of chemicals.  
5 Five iterative phases of Tier 2 reliability testing were performed to assess Tier 2 as the methodology  
6 evolved. These assessments involved over 130 unique chemicals. Results of these evaluations show that  
7 Tier 2 OEBs appropriately reflect the toxicity of a chemical. Tier 2 OEBs include the OEL or are more  
8 protective than the OEL for 98% of chemicals tested. In summary, the results from the evaluation  
9 exercises demonstrate that the occupational exposure banding process operates as expected, and can be a  
10 useful tool to evaluate chemicals without OELs. Special consideration should be given when banding  
11 substances comprised of a mixture of two or more chemicals. Other situations that warrant special  
12 considerations, such as nanoparticles, are described in detail in this document.

13

14 The number of chemicals that lack authoritative OELs is substantial, and risk management guidance for  
15 these chemicals is needed. Occupational exposure banding is one additional tool that can be used to  
16 provide guidance. An OEB provides more than a range of exposures that is expected to be protective of  
17 worker health. Rather, an OEB can be utilized to identify potential health effects and target organs,  
18 identify health risks that affect health communication, inform implementation of control interventions  
19 and preparedness plans, inform medical surveillance decisions, and provide critical information quickly.  
20 This document fully details the use and application of this process and provides a summary of efforts  
21 taken to evaluate its effectiveness and usability.

## 1 Abbreviations

2	ACGIH	American Conference of Governmental Industrial Hygienists®
3	ATSDR	Agency for Toxic Substances and Disease Registry
4	BMD	Benchmark Dose
5	BMCL	Benchmark Concentration Lower Bound
6	BMDL	Benchmark Dose Lower Bound
7	CalEPA	California Environmental Protection Agency
8	CalOEHHA	State of California Office of Environmental Health Hazard Assessment
9	Cal/OSHA	California Occupational Safety and Health Administration
10	CAS	Chemical Abstract Service
11	CFR	Code of Federal Regulations
12	CICADs	Concise International Chemical Assessment Documents
13	DNEL	Derived No Effect Level
14	EDS	Endpoint Determinant Score
15	EHC	Environmental Health Criteria
16	ECHA	European Chemicals Agency
17	ER GV	Emergency Response Guide Value
18	EU	European Union
19	GHS	Globally Harmonized System of Classification and Labelling of Chemicals
20	GPMT	Guinea Pig Maximization Test
21	H-code	Hazard Code
22	HCS	Hazard Communication Standard
23	HSDB	Hazardous Substance Data Bank
24	IARC	International Agency for Research on Cancer
25	IDLH	Immediately Dangerous to Life or Health
26	IRIS	U.S. EPA Integrated Risk Information System
27	ISO	International Standards Organization
28	ITER	International Toxicity Estimates for Risk
29	IUR	Inhalation Unit Risk
30	kg	Kilogram

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1	LC <sub>50</sub>	Median Lethal Concentration
2	LD <sub>50</sub>	Median Lethal Dose
3	LLNA	Local Lymph Node Assay
4	LOAEL	Lowest Observed Adverse Effect Level
5	mg/kg	Milligrams per Kilogram
6	mg/m <sup>3</sup>	Milligrams per Cubic Meter of Air
7	MRL	Minimal Risk Level
8	NIOSH	National Institute for Occupational Safety and Health
9	NLM	National Library of Medicine
10	NOAEL	No Observed Adverse Effect Level
11	NTP	National Toxicology Program
12	OEB	Occupational Exposure Band
13	OEB <sub>ER</sub>	Emergency Response Band
14	OECD	Organisation for Economic Cooperation and Development
15	OEL	Occupational Exposure Limit
16	OSHA	Occupational Safety and Health Administration
17	PEL	Permissible Exposure Limit
18	POD	Point of Departure
19	ppm	Parts per Million
20	REACH	Registration, Evaluation, Authorization and Restriction of Chemicals (European
21		Chemicals Agency)
22	REL	Recommended Exposure Limit
23	RfC	Reference Concentration
24	RfD	Reference Dose
25	RoC	U.S. National Toxicology Program Report on Carcinogens
26	SDS	Safety Data Sheet
27	SF	Slope Factor
28	SIDS	Screening Information Dataset
29	STOT-RE	Specific Target Organ Toxicity-Repeated Exposure
30	TC <sub>05</sub>	Tumorigenic Concentration for 5% of the population

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1	TD <sub>05</sub>	Tumorigenic Dose for 5% of the population
2	TDC	Tolerable Daily Concentration
3	TDI	Tolerable Daily Intake
4	TDS	Total Determinant Score
5	TI	Tolerable Intake
6	TLV	Threshold Limit Value®
7	TWA	Time-Weighted Average
8	U.S. EPA	U.S. Environmental Protection Agency
9	WEEL	Workplace Environmental Exposure Level®
10	WHO	World Health Organization

# 1 Glossary

2 **Acute toxicity:** refers to those adverse effects occurring following oral or dermal administration of a  
3 single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours

4 **Aspiration toxicity:** severe acute effects such as chemical pneumonia, varying degrees of pulmonary  
5 injury or death following aspiration

6 **Aspiration:** the entry of a liquid or solid directly through the oral or nasal cavity, or indirectly from  
7 vomiting, into the trachea and lower respiratory system

8 **Carcinogenicity:** the ability of a chemical substance or a mixture of chemical substances to induce  
9 tumors, increase tumor incidence and/or malignancy or shorten the time to tumor occurrence

10 **Control banding:** a strategy that groups workplace risks into control categories or bands based on  
11 combinations of hazard and exposure information. The following four main control bands have been  
12 developed for exposure to chemicals by inhalation:

- 13  
14 Band 1: Use good industrial hygiene practice and general ventilation.  
15 Band 2: Use local exhaust ventilation.  
16 Band 3: Enclose the process.  
17 Band 4: Seek expert advice.

18  
19 This qualitative strategy to assess and manage risk focuses resources on exposure controls and describes  
20 how strictly a risk needs to be managed.

21  
22 **Corrosive to metals:** a substance or a mixture that by chemical action will materially damage, or even  
23 destroy, metals

24 **Endpoint:** a marker of response from exposure to a physical, health, or environmental hazard

25 **Explosive:** a solid or liquid that is in itself capable by chemical reaction of producing gas at such a  
26 temperature and pressure and at such a speed as to cause damage to the surroundings

27 **Eye irritation:** changes in the eye following the application of a test substance to the front surface of the  
28 eye; that are fully reversible within 21 days of application

29 **Flammable aerosols:** any gas compressed, liquefied or dissolved under pressure within a non-refillable  
30 container made of metal, glass or plastic, with or without a liquid, paste or powder that is flammable

31 **Flammable gas:** a gas having a flammable range in air at 20°C and a standard pressure of 101.3 kPa

32 **Flammable liquid:** a liquid having a flash point of not more than 93°C

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- 1 **Flammable solid:** a solid that is readily combustible, or may cause or contribute to fire through friction
- 2 **Gases under pressure:** gases that are contained in a receptacle at a pressure not less than 280 Pa at 20°C  
3 or as a refrigerated liquid
- 4 **Germ cell mutagenicity:** an agent that can cause permanent changes to the amount or structure of the  
5 genetic material in a germ cell (an ovum or sperm cell, or one of their developmental precursors),  
6 thereby potentially resulting in the transfer of the mutation to the offspring of an exposed recipient,  
7 animal or human
- 8 **GESTIS substance database:** a database of the German Social Accident Insurance that contains  
9 approximately 8,000 chemicals with toxicological data, physical and chemical properties, regulations,  
10 and hazard statements, codes, and categories  
11
- 12 **Hazard category:** the division of criteria within each hazard class (e.g., oral acute toxicity) includes five  
13 hazard categories, and “flammable liquids” includes four hazard categories. These categories compare  
14 hazard severity within a hazard class and should not be taken as a comparison of hazard categories more  
15 generally.
- 16 **Hazard class:** the nature of the physical, health or environmental hazard, e.g., flammable solid,  
17 carcinogen, oral acute toxicity
- 18 **Hazard code:** alphanumeric code used to designate a hazard statement
- 19 **Hazard statement:** a statement assigned to a hazard class and category that describes the nature of the  
20 hazards of a chemical or chemical mixture, including, where appropriate, the degree of hazard
- 21 **Mixture:** solutions composed of two or more substances in which they do not react
- 22 **Mutagen:** an agent giving rise to an increased occurrence of mutations in populations of cells and/or  
23 organisms
- 24 **Occupational exposure banding:** (also called hazard banding) a systematic process using qualitative or  
25 quantitative hazard information on selected health effect endpoints to identify potential inhalation-based  
26 exposure ranges or categories for guiding occupational risk assessment and risk management
- 27 **Occupational exposure limit:** Levels of exposure that most employees may be exposed to for up to 10  
28 hours per day, 40 hours per week, for a working lifetime, without experiencing adverse health effects.
- 29 **Organic peroxide:** an organic liquid or solid that contains the bivalent -O-O- structure and may be  
30 considered a derivative of hydrogen peroxide, where one or both of the hydrogen atoms have been  
31 replaced by organic radicals

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- 1 ***Oxidizing gas:*** any gas that may, usually by providing oxygen, cause or contribute to the combustion of  
2 other material more than air does
- 3 ***Oxidizing liquid:*** a liquid that, while in itself is not necessarily combustible, may, generally by yielding  
4 oxygen, cause or contribute to the combustion of other material
- 5 ***Oxidizing solid:*** a solid that, while in itself not necessarily combustible, may, generally by yielding  
6 oxygen, cause or contribute to the combustion of other material
- 7 ***Pyrophoric liquid:*** a liquid that, even in small quantities, is liable to ignite within 5 minutes of coming  
8 into contact with air
- 9 ***Pyrophoric solid:*** a solid that, even in small quantities, is liable to ignite within 5 minutes of coming into  
10 contact with air
- 11 ***Reproductive toxicity:*** the ability of a substance to induce adverse effects on sexual function or fertility  
12 in adult males or females, or adverse developmental effects in offspring
- 13 ***Respiratory sensitizer:*** a substance that induces hypersensitivity of the airways following inhalation of  
14 the substance
- 15 ***Self-heating substance:*** a solid or liquid, other than a pyrophoric substance, which, by reaction with air  
16 and without energy supply, is liable to self-heat. This endpoint differs from a pyrophoric substance in that  
17 it will ignite only when in large amounts (kilograms) and after long periods of time (hours or days).
- 18 ***Self-reactive substance:*** a thermally unstable liquid or solid liable to undergo a strongly exothermic  
19 thermal decomposition even without participation of oxygen (air)
- 20 ***Serious eye damage:*** the production of tissue damage in the eye, or serious physical decay of vision,  
21 following application of a test substance to the front surface of the eye, which is not fully reversible  
22 within 21 days of application
- 23 ***Skin corrosion:*** the production of irreversible damage to the skin following the application of a test  
24 substance for up to 4 hours
- 25 ***Skin irritation:*** the production of reversible damage (excluding allergic responses) to the skin following  
26 the application of a test substance for up to 4 hours
- 27 ***Skin sensitizer:*** a substance that will induce an allergic response following skin contact
- 28 ***Specific target organ toxicity – repeated exposure:*** all significant health effects, not otherwise specifically  
29 included in the Globally Harmonized System of Classification and Labeling of Chemicals (GHS) that can  
30 impair function, both reversible and irreversible, immediate and/or delayed after repeated exposure to a  
31 substance

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1 ***Specific target organ toxicity – single exposure:*** all significant health effects, not otherwise specifically  
2 included in the GHS that can impair function, both reversible and irreversible, immediate and/or delayed  
3 after a single exposure to a substance

4 ***Substance:*** a chemical element and its compounds in the natural state or obtained by any production  
5 process, including any additive necessary to preserve the stability of the product and any impurities  
6 deriving from the process used, but excluding any solvent that may be separated without affecting the  
7 stability of the substance or changing its composition

8 ***Substances that, in contact with water emit flammable gases:*** solids or liquids that, by interaction with  
9 water, are liable to become spontaneously flammable or to give off flammable gases in dangerous  
10 quantities

11 ***Total determinant score:*** a quantitative measure of data sufficiency of a compound for banding in Tier 2  
12 of the evaluation. Total determinant score comprises the sum of component scores assigned for the  
13 availability of endpoint-specific toxicological information. A threshold of 30 (out of a maximum  
14 possible score of 125) marks a chemical-specific dataset as sufficient for banding in Tier 2.

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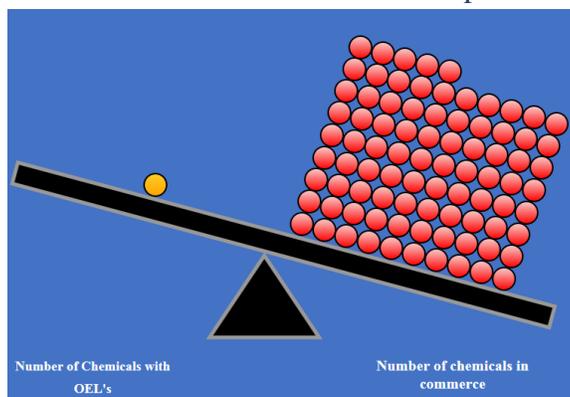
# Chapter 1 : Introduction to Occupational Exposure Banding

## 1.0. Occupational Exposure Banding: Definition

Occupational exposure limits (OELs) have been an important component of the practice of occupational hygiene for decades [Cook 1987; Schulte et al. 2010; Nikfar and Malekiran 2014; Deveau et al. 2015; Skowroń and Czerczak 2015]. Occupational hygienists develop and implement control strategies largely based on the relevant OELs that are available to them. Exposures to chemicals at concentrations above their OEL are considered unsafe, and hygienists act to ensure that workers are not exposed to concentrations of hazardous chemicals that exceed their designated OELs. Unfortunately, the rate that chemicals have been introduced into commerce has significantly outpaced the development of authoritative (i.e., governmental, consensus, or peer reviewed) OELs [Michaels 2014]. The U.S. Environmental Protection Agency (EPA) reports that the Toxic Substances Control Act (TSCA) Chemical Substance Inventory contains over 85,000 chemicals [EPA 2015], yet only about 1,000 chemicals have been assigned at least one authoritative OEL. (See Figure 1-1.)

As NIOSH and other government, international, and professional agencies continue to develop new OELs and update existing OELs, guidance for the thousands of chemicals that currently lack reliable exposure limits is needed. The occupational exposure banding process uses chemical toxicity data to assign a range of concentrations to which chemical exposures should be controlled. The output of the occupational exposure banding process is an occupational exposure band (OEB) that defines the range of exposures expected to be protective of worker health. Thus, occupational exposure banding is one of a number of strategies used to address worker and responder safety and health when the time, data, and resources needed for OEL development are not available.

Figure 1-1: Chemicals in Commerce vs. Chemicals with Occupational Exposure Limits



26

18

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1 Sometimes referred to as hazard banding or health hazard banding, occupational exposure  
2 banding is defined as a systematic process that uses qualitative or quantitative hazard  
3 information on selected health effect endpoints to identify potential inhalation-based exposure  
4 ranges or categories for guiding occupational risk assessment and risk management. In the  
5 context of this document, the term exposure refers to human contact with a chemical agent in the  
6 work environment. For chemical compounds, exposure can occur through inhalation, ingestion,  
7 or through contact with the skin, eye, mucous membranes, or other parts of the body. The term  
8 *hazard* is used herein to describe potential threats to life, health, or well-being. Chemical hazards  
9 have the potential to cause harm or adverse effects to individuals who are exposed to them. The  
10 purpose of occupational exposure banding is to reduce the risk to workers who are exposed to  
11 chemicals in the workplace. Risk is defined as the probability that a person will experience  
12 adverse effects after exposure to chemical hazards. Occupational exposure banding can be an  
13 effective tool to assess and manage risk to workers.

14 The concept of using hazard-based categories to communicate potential health concerns, alert  
15 employers and workers to the need for risk management, and even to inform exposure control  
16 requirements is not new. Numerous hazard classification and category-based systems have seen  
17 extensive use in the occupational setting [Zalk and Nelson 2008; Egeghy et al. 2011; Shin et al.  
18 2014]. Such systems are deeply embedded in occupational hygiene practice, particularly in the  
19 pharmaceutical industry, and are also elements of well-developed, modern hazard  
20 communication programs (e.g., UN 2013 Globally Harmonized System of Classification and  
21 Labelling of Chemicals).

22 As previously mentioned, most guidance on chemical hazards has been in the form of OELs  
23 rather than OEBs. The science and art of evaluating chemical hazards in the workplace and  
24 determining levels of exposure (i.e., OELs) that are associated with minimal risk of adverse  
25 health effects have a mature history in the promotion of occupational safety and health [Binks  
26 2003; Laszcz-Davis et al. 2014]. Despite this history, derivation of OELs remains a resource  
27 intensive process driven by the need for exposure data, toxicology data, risk assessment  
28 methodology, and other considerations [Schulte et al. 2010]. Consequently, the number of  
29 chemicals for which government, consensus, or peer-reviewed OELs have been published in the  
30 last half-century of practice is relatively low: roughly 2,000 OELs covering approximately 1000  
31 chemicals. In many cases, multiple organizations have assigned different OELs to the same  
32 chemical, making the number of chemicals that have been assigned an OEL even fewer. At the  
33 same time, the Occupational Safety and Health Administration (OSHA) has estimated that  
34 80,000 hazardous chemicals are currently used in the United States, and over 40 million  
35 employees are now potentially exposed to hazardous chemicals in over 5 million workplaces  
36 [OSHA 2012]. The characterization of the potential adverse health effects of chemical and

## DRAFT

1 physical agents is one of the foundations of occupational hygiene as a public health practice  
2 [OSHA 1998]. Therefore, strategies for expedited assessment and characterization of chemical  
3 hazards are needed to inform occupational risk management decisions.

4 The National Institute for Occupational Safety and Health (NIOSH) occupational exposure  
5 banding process guides a user through the evaluation and selection of critical health hazard  
6 information to identify the appropriate OEB from among five categories of severity of health  
7 outcomes (bands A to E; band A is least severe and band E is most severe). Thus, the OEBs  
8 reflect toxicity potency ranges where band A chemicals have the lowest health hazard potential  
9 (and thus higher exposure ranges), and band E chemicals have the highest recognized health  
10 hazard potential Figure 1-2[McKernan et al. 2016].

11 Figure 1-2: Occupational exposure bands [McKernan et al. 2016].



12 Occupational exposure banding aligns with the professional practice framework of anticipation,  
13 recognition, evaluation, control, and confirmation of protection from health hazards [Laszcz-  
14 Davis et al. 2014; Jahn et al. 2015]. Furthermore, occupational exposure banding will assist in  
15 the qualitative aspects of risk management by providing relative hazard bands for chemicals  
16 being reviewed [OSHA 1998]. Through a consistent and documented process for characterizing  
17 chemical hazards according to recommended OEBs, timely and well-informed risk management  
18 decisions can be made for chemicals lacking OELs. This process can also be used to prioritize  
19 chemicals for which OELs should be established [McKernan and Seaton 2014]. In addition, an  
20 occupational exposure banding framework can be used to identify additional data needs to  
21 establish OELs. Finally, occupational exposure banding packages information in a way that  
22 facilitates hazard communication and provides critical information quickly. Following the  
23 banding process allows the user to identify health risks that affect health communication, inform  
24 implementation of control interventions, and inform medical surveillance decisions. Given these  
25 considerations, NIOSH sought to develop and evaluate an occupational exposure banding  
26 framework and supporting guidance for use in assessing and characterizing chemical hazards in  
27 the workplace. This document provides the NIOSH process as the result of that effort.

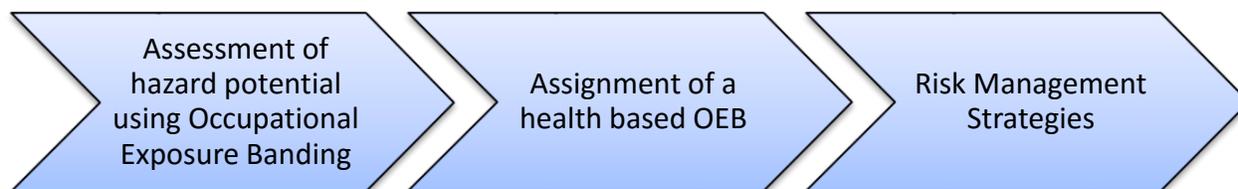
28 Although the NIOSH occupational exposure banding process provides exposure ranges for each  
29 band that can serve as a guide for risk management, it is important to distinguish the  
30 occupational exposure banding process from the concept of control banding. For OEBs, the  
31 process uses only hazard-based data (e.g., studies on human health effects or toxicology studies)

## DRAFT

1 to identify an overall level of hazard potential and associated airborne concentration range for  
2 chemicals with similar hazard profiles. While the occupational hygienists can use output of this  
3 process to make risk management and exposure control decisions, the process does not supply  
4 such recommendations directly. In contrast, control banding methods, such as the United  
5 Kingdom Health and Safety Executive Control of Substances Hazardous to Health, essentially  
6 link hazards to specific control measures [AIHA 2007; Zalk and Nelson 2008; NIOSH 2009c;  
7 Zalk et al. 2010; Beaucham et al. 2012; HSE 2013] (see also  
8 <http://www.hse.gov.uk/coshh/basics.htm>). For this reason the occupational exposure banding  
9 process can ultimately be applied for informing risk management and control decisions, but in  
10 itself is not control banding, as demonstrated in Figure 1-3.

11 The control banding approach has utility in the field, but has some limitations. The UK method,  
12 for example, provides one of four very general control recommendations (use general ventilation,  
13 use local exhaust ventilation, enclose the process, or seek expert advice) based on simplistic  
14 inputs from the user. The occupational exposure banding method was developed to ensure a  
15 rigorous scientific foundation that has been evaluated to ensure confidence in the OEB  
16 assignments. The development of OEBs require more sophisticated inputs, and thus tends to a  
17 more refined output. Additionally, the purpose of OEBs is not to directly link to a control  
18 strategy, but rather define a range of exposures to protect worker health. The information  
19 provided by OEBs, in concert with exposure assessment, can be used to measure the  
20 effectiveness of the controls that are in place, and whether additional controls would be  
21 advisable.

22 Figure 1-3: Potential use of occupational exposure banding for the development of risk management  
23 strategies.



### 24 1.1. History of Occupational Exposure Banding Applications

25 Companies with significant in-house occupational hygiene, toxicology, chemistry, and  
26 occupational medicine expertise have used the hazard banding approach for decades to establish  
27 exposure control limits or ranges for new chemicals for which no full OEL has been developed.  
28 Although use of hazard banding techniques was already well established at the time, an early

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1 journal publication on the approach highlighted application of “performance-based exposure  
2 control limits” in the pharmaceutical sector [Naumann et al. 1996].

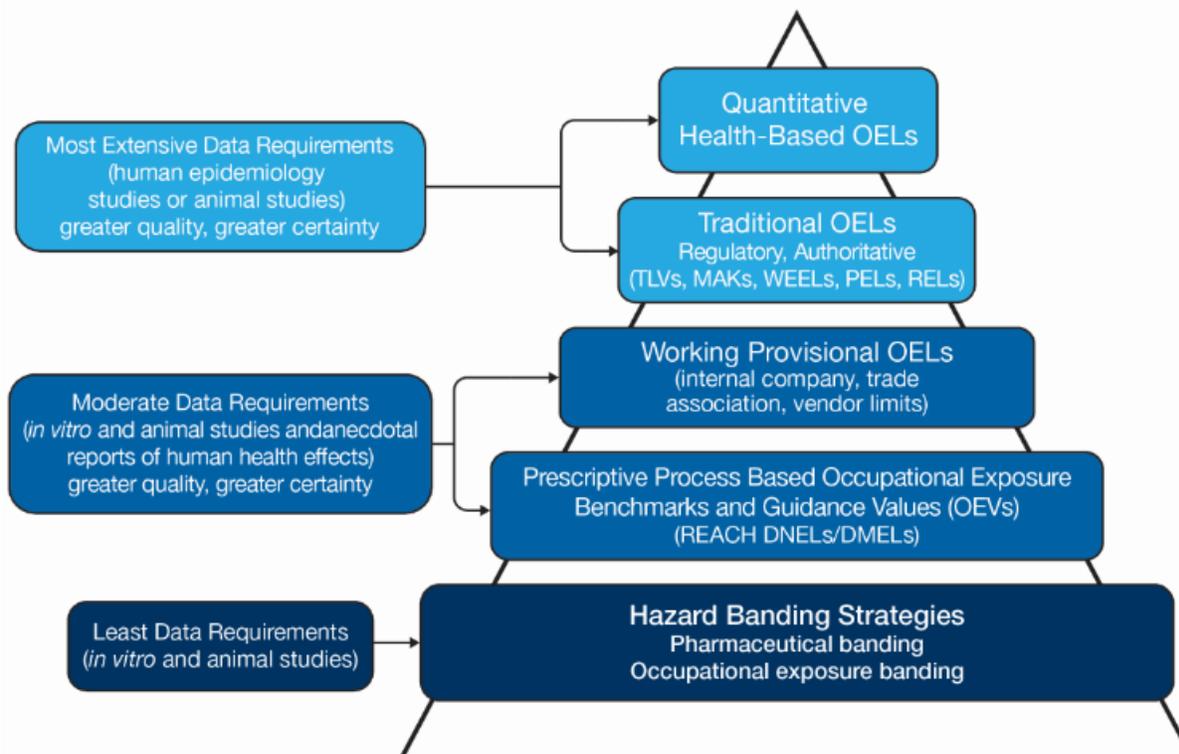
3 The hazard banding technique remains well accepted among the pharmaceutical and larger  
4 chemical company risk assessment communities. The development of OEBs, health-hazard  
5 categories, hazard groups, and hazard-based exposure control limits indicates a desire within the  
6 health and safety community to share information about risk in ways that can be applied more  
7 broadly within the occupational hygiene field. The need for this effort is supported by the  
8 observation that most chemicals in commerce and thus, encountered in our workplaces, have no  
9 published occupational exposure guidelines. This paucity of chemical-specific guidance coupled  
10 with the new accessible process provides an immediate and opportune environment for  
11 developing additional risk assessments. In addition to the OEBs providing interim risk  
12 management guidance for chemicals without OELs, the occupational exposure banding process  
13 can be used to (1) array the available hazard data and identify key data gaps, (2) prioritize  
14 chemicals for full OEL development based on data availability and overall hazard profile, and  
15 (3) conduct a quality assurance review for overall consistency in OEL derivation.

16 The call for greater utility of occupational exposure banding has become part of the discussion in  
17 the occupational hygiene community [Ripple 2009] and has also been adopted by volunteer OEL  
18 setting committees such as the Workplace Environmental Exposure Limits (WEEL<sup>®</sup>) Committee  
19 [Maier 2009]. The OEB concept has also gained emphasis as part of a continuum of exposure  
20 guide values for occupational risk assessment – a concept being formalized in the occupational  
21 hygiene community as part of the hierarchy of OELs [Laszcz-Davis et al. 2014; McKernan and  
22 Seaton 2014; Deveau et al. 2015; Jahn et al. 2015] (see Figure 1-4). In this hierarchy, OELs are  
23 categorized based on how much toxicological and epidemiological data are required to develop  
24 each limit. Quantitative, health-based OELs are at the top of the hierarchy. These OELs have the  
25 most extensive data requirements and are often considered the most precise. The amount and  
26 quality of data to form quantitative, health-based OELs are not always available for every  
27 potentially hazardous chemical, so alternate strategies must be employed to develop health-  
28 protective limit values. These alternative methods are found further down the hierarchy as the  
29 data requirements are reduced. It is important to note that traditional OELs often vary in their  
30 data requirements based on when they were assigned and the process used to develop them.  
31 Consequently, traditional OELs may be appropriately categorized into several levels of the  
32 hierarchy, depending on a number of factors such as data and reporting quality. At the base of  
33 the pyramid are health hazard banding strategies, including the NIOSH process to occupational  
34 exposure banding. Because the data requirements to determine an OEB are much lower, the  
35 precision of the band is also reduced; therefore, occupational exposure banding strategies tend to

## DRAFT

1 result in lower concentration ranges than other processes for developing OELs [Jankovic 2007;  
2 Laszcz-Davis et al. 2014; Deveau et al. 2015].

3 Figure 1-4: Hierarchy of controls. Adapted from [Laszcz-Davis et al. 2014; Jahn et al. 2015].



4

### 5 1.2. Features of the NIOSH Occupational Exposure Bands

6 The NIOSH occupational exposure banding process shares similar scientific underpinnings with  
7 the processes used by many organizations. Key aspects of the process shared by most  
8 organizations include:

- 9
- 10 • Collecting the data to facilitate evaluation of individual health effect endpoints
  - 11 • Comparing the hazard data for each endpoint to criteria (qualitative or quantitative) for that endpoint
  - 12 • Identifying the endpoints that appear to generate the greatest level of hazard leading to selection of an overall hazard band
  - 13 • Assigning the band and associated air concentration range.
- 14

15 To date, few published processes or resources facilitate harmonization and broader use among  
16 the occupational hygiene community. NIOSH seeks to address this deficit by providing a  
17 comprehensive exposure banding process with broad application and utility.

## DRAFT

1 Some key features of the NIOSH occupational exposure banding process distinguish it from  
2 other common hazard classification and category-based systems. One key feature is the use of  
3 the OEB as a tool for considering the overall hazard profile for multiple health hazard endpoints  
4 at the same time. The band-specific technical criteria apply to nine potential toxicological or  
5 human health outcomes: (1) carcinogenicity, (2) reproductive toxicity, (3) specific target organ  
6 toxicity, (4) genotoxicity, (5) respiratory sensitization (6) skin sensitization, (7) acute toxicity,  
7 (8) skin corrosion and irritation, and (9) eye damage/irritation. The integration of each of the  
8 hazards yields the identification of an OEB that considers the severity of hazard posed for  
9 numerous health endpoints relevant to worker health. The overall band is assigned on the basis of  
10 protection against the most severe effects. This process goes beyond hazard classification  
11 systems such as the Globally Harmonized System of Classification and Labelling of Chemicals  
12 (GHS) that identify each relevant hazard independently without providing an overall assessment  
13 to guide risk assessment and management. However, NIOSH OEB endpoints are aligned with  
14 GHS, and the process relates potency of each occupational exposure banding endpoint to GHS  
15 hazard statements and categories, when possible. The NIOSH occupational exposure banding  
16 process also is more comprehensive than systems such as the hazardous materials information  
17 system process, which gives a single integrated hazard category based on limited, usually acute  
18 toxicity or lethality, endpoints. The OEB has improved utility for hazard communication  
19 compared to these other systems because it highlights the endpoints that are most likely to affect  
20 overall worker risk.

21 A second key feature of the NIOSH occupational exposure banding process is the linkage of  
22 hazard-based categories (i.e., bands) to airborne concentration ranges. The corresponding  
23 exposure concentration ranges for each of the five NIOSH OEBs are designated by the letters A  
24 through E and are listed in Table 1-1. This process improves the utility of the hazard-based  
25 system by providing a target air concentration range that can be used for traditional occupational  
26 risk management purposes such as identifying the adequacy of exposure control strategies. These  
27 exposure ranges are intended to reflect the range of full-shift OELs that would be expected for a  
28 chemical with a similar hazard profile. Because the OEBs are often based on smaller health  
29 effects data sets or less detailed analyses than those of traditional OELs, they should be used  
30 with this limitation in mind for supporting risk management decisions.

31

## DRAFT

1 **Table 1-1: Airborne concentration ranges associated with occupational exposure bands**  
2

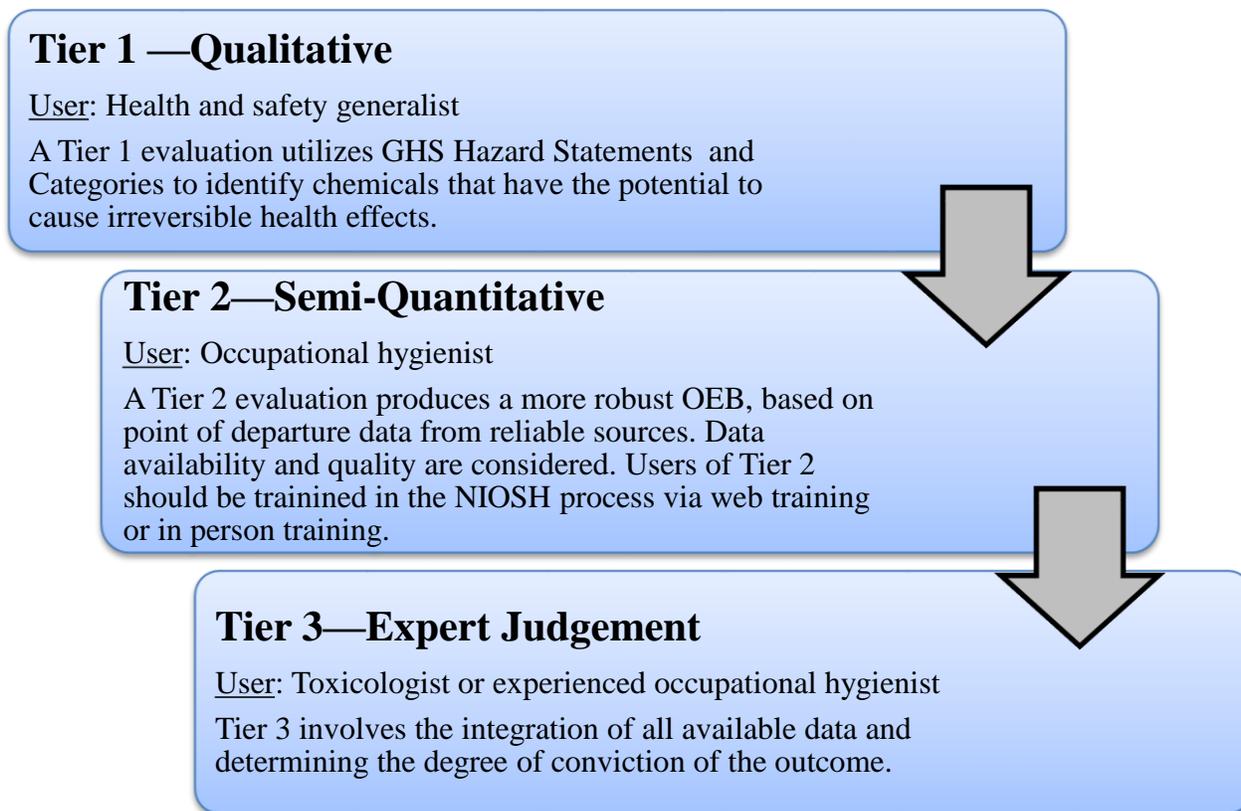
Occupational Exposure Band	Airborne Target Range for Particulate Concentration (mg/m <sup>3</sup> )	Airborne Target Range for Gas or Vapor Concentration (ppm)
A	>10mg/m <sup>3</sup>	>100 ppm
B	>1 to 10 mg/m <sup>3</sup>	>10 to 100 ppm
C	>0.1 to 1 mg/m <sup>3</sup>	>1 to 10 ppm
D	>0.01 to 0.1 mg/m <sup>3</sup>	>0.1 to 1 ppm
E	≤0.01 mg/m <sup>3</sup>	≤0.1 ppm

3  
4 As currently practiced, hazard banding requires a significant amount of technical expertise in  
5 industrial hygiene, which limits the size of the immediate user community. To address this  
6 limitation, the NIOSH process uniquely provides a three-tiered assessment process that allows  
7 for the application of the technique with traditional occupational hygiene expertise along with  
8 the option of more in-depth processes in consultation with specialists in occupational medicine  
9 and toxicology (refer to Figure 1-5). The three tiers in the process include the following:

- 10 • **Tier 1:** Qualitative OEB assignment based on GHS. Tier 1 involves assigning the OEB  
11 based on criteria aligned with specific GHS hazard codes and categories. It is intended  
12 for individuals with basic toxicology knowledge. Chemicals with potential for  
13 irreversible health effects at relatively low doses warrant assigning band D or band E.  
14 Chemicals that are likely to cause reversible health effects are categorized in band C.  
15 Bands A and B are not assigned in Tier 1. Since there are relatively low data  
16 requirements for Tier 1, there is not enough information to suggest exposure ranges for  
17 chemicals Bands A and B in Tier 1. In general, Tier 1 can be used as a quick screening  
18 method, but NIOSH recommends going to Tier 2 if the user expertise and data are  
19 available.
- 20 • **Tier 2:** Semi-quantitative OEB assignment based on secondary sources: Tier 2 involves  
21 assigning the OEB on the basis of key findings from prescribed literature sources,  
22 including use of data from specific types of studies. It is intended for individuals with  
23 intermediate toxicology knowledge. Tier 2 is more quantitative in nature than Tier 1.  
24 Individuals performing Tier 2 assessments will need to determine a point of departure by  
25 using the instructions that are provided for endpoints to support assigning chemicals into  
26 bands A, B, C, D, or E.
- 27 • **Tier 3:** Expert Judgement: OEB based on primary sources and expert judgement: Tier 3  
28 involves the use of expert judgement to assign the OEB based on in-depth review of  
29 health effects studies. It should only be performed by individuals with advanced  
30 toxicology knowledge. Tier 3 involves a more quantitative comprehensive evaluation of

1 the scientific information and requires integration of all available data to determine the  
2 band assignment.

3 Figure 1-5: The three tiers of the NIOSH occupational exposure banding process



4  
5 A third key feature of the NIOSH process is the incorporation of technical features that address  
6 challenges in traditional applications of the occupational exposure banding process. One such  
7 feature is the inclusion of a process for systematic decision making to determine if the existing  
8 data for a chemical are adequate to assign a band with reasonable confidence. The approach used  
9 in the occupational exposure banding process is to include the calculation of a total determinant  
10 score (TDS) for the database being evaluated. TDS reflects the availability of qualitative and  
11 quantitative data for each endpoint. The presence or absence of data for each health endpoint  
12 results in an endpoint determinant score (EDS), and the TDS is the sum of the EDS values. The  
13 TDS is a weighted score that considers both the endpoints for which data are available and the  
14 overall relevance or impact to the assessment of risk. For example, the occupational exposure  
15 banding process provides for a systematic documentation of data availability and whether data  
16 are available for a sufficient array of separate endpoints to derive a band assignment. This  
17 process has the following key uses:

## DRAFT

- 1 • Documents the data availability for each of the nine potential toxicological or human  
2 health outcomes. This process can guide new data development priorities.
- 3 • Documents whether data are sufficient to assign a band. If not, the hierarchy of OEL  
4 concept can be used, and alternative techniques such as the threshold of toxicological  
5 concern [Dolan et al. 2005] might be used.

### 6 1.3. Evaluation of the Process

7 Occupational exposure banding, like other hazard or dose-response tools for occupational risk  
8 assessment, is one of many processes that occupational hygienists use for evaluation of  
9 workplace hazards. The OEB process has been developed so that it closely aligns with  
10 anticipated OELs for chemicals with similar hazard profiles. To build confidence in occupational  
11 exposure banding, the alignment between the OEBs and current OELs was evaluated. OEBs  
12 assigned to chemicals using the NIOSH methodology are intended to be at least as protective as  
13 an OEL assigned to the chemical would be. In this document, an OEB is described as being at  
14 least as protective as, or more protective than, the lowest OEL when the concentration range of  
15 the OEB includes the OEL or is lower than the OEL. Typically, lower exposures are thought to  
16 be more protective of worker health, and thus the word protective is used herein. In a previous  
17 study, [Brooke 1998] evaluated the effectiveness of a new UK scheme that utilizes toxicological  
18 hazard information to assign chemicals to hazard bands. The UK scheme utilized R-phrases,  
19 which were assigned under the European Union (EU) classification scheme, to assign chemicals  
20 to one of five toxicological hazard bands (A-E). Like the NIOSH process, each band represents a  
21 different target airborne exposure range for dusts and vapors. In the UK study, 111 chemicals  
22 were banded using the UK scheme and the target airborne exposure concentration range  
23 associated with the hazard band for a specific chemical was compared with the numerical value  
24 of the OEL. Results of this study showed that for 98% of the chemicals the target exposure for  
25 hazard banding was lower than the OEL.

26  
27 In this current effort, NIOSH has compared the Tier 1 and Tier 2 banding results for 600  
28 chemicals with existing OELs. More specifically, OEBs were compared to the lowest available  
29 concentration values among several governmental, consensus, and peer reviewed OELs. A  
30 detailed description of the evaluation results is available in Chapter 5. The overall of Tier 1  
31 bands that were at least as protective as the OEL was 91.5% (combined vapor and particulate).

# Chapter 2 : Banding Chemicals with GHS Information: The Tier 1 Occupational Exposure Banding Process

## 2.0. Technical Approach

The Tier 1 technical criteria use hazard phrases, codes, and categories of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). GHS covers most hazardous chemicals and provides a uniform approach for communicating hazards related to chemical exposures. Under GHS, chemicals are assigned standardized hazard codes and categories based on their known toxicological characteristics [UNECE 2013]. As shown in Table 2-1, Tier 1 relies on the use of this information to assign OEBs. Bands A and B are not assigned in Tier 1. Since there are relatively low data requirements for Tier 1, there is not enough information to suggest higher exposure ranges for chemicals banded in Tier 1. This cautious approach decreases the likelihood of allowing overexposures. The GHS hazard codes and categories assigned to a chemical of interest can be found on an OSHA-compliant safety data sheet (SDS), as well as in a number of databases that address chemical safety. Detailed information on GHS hazard codes and categories is found in Section 2.1.

**Table 2-1: Tier 1 Criteria Overview: GHS Hazard Codes and Categories for Tier 1 Hazard Banding\***

Preliminary NIOSH Tier 1 criteria		C	D	E
OEL ranges	Particle	> 0.1 to ≤ 1 milligrams per cubic meter of air (mg/m <sup>3</sup> )	> 0.01 to ≤ 0.1 mg/m <sup>3</sup>	≤ 0.01 mg/m <sup>3</sup>
	Vapor	> 1 to ≤ 10 parts per million (ppm)	> 0.1 to ≤ 1 ppm	≤ 0.1 ppm
Acute toxicity		H301 Category 3	H300 Category 2	H300 Category 1
		H302 Category 4		
		H331 Category 3		
		H332 Category 4	H330 Category 2	H330 Category 1
		H311 Category 3	H310 Category 2	H310 Category 1
		H312 Category 4		

19

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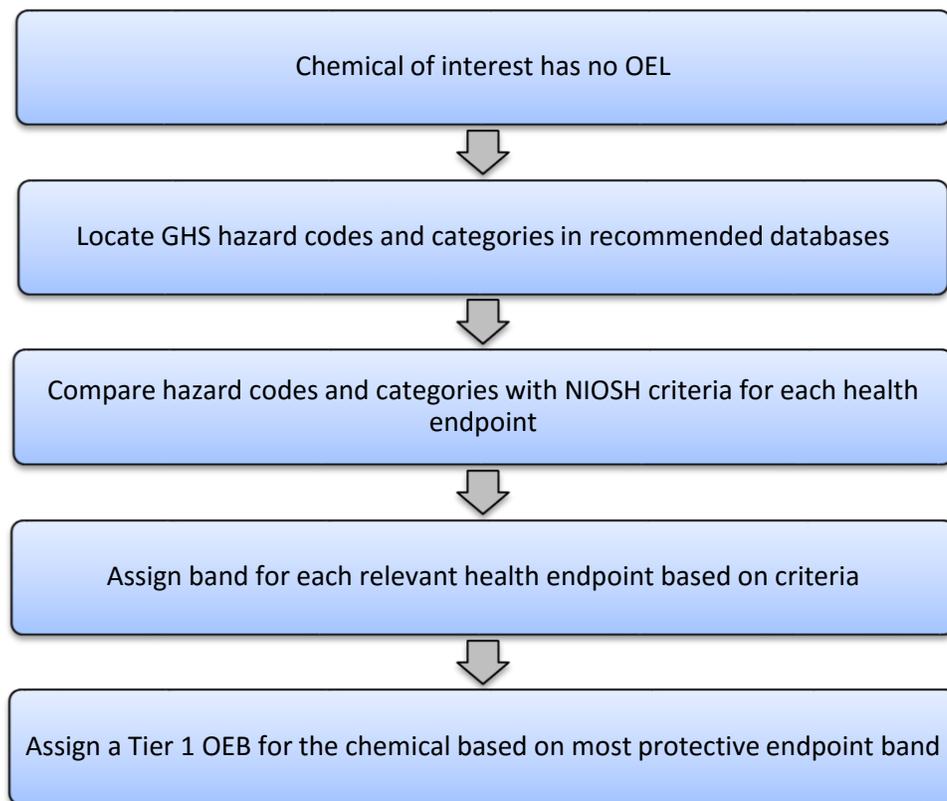
Skin corrosion/ irritation	H315 Category 2	—	H314 Category 1, 1A, 1B, or 1C
Serious eye damage/ eye irritation	H319 Category 2, 2A or 2B	—	H318 Category 1
Respiratory and skin sensitization	H317 Category 1B (skin)	H317 Category 1 or 1A	—
	—	H334 Category 1B	H334 Category 1 or 1A
Genotoxicity	—	H341 Category 2	H340 Category 1, 1A or 1B
Carcinogenicity	—	—	H350 Category 1, 1A, or 1B
	—	—	H351 Category 2
Reproductive Toxicity	H361 (including H361f, H361d, and H361fd) Category 2	H360 (including H360f, H360d, and H360fd) Category 1B	H360 (including H360f, H360d, and H360fd) Category 1 or 1A
Specific target organ toxicity	H371 Category 2	—	H370 Category 1
	H373 Category 2	—	H372 Category 1

1 *\*Note that the following hazard codes will not be used for Tier 1 Banding: H200's, H303, H305, H313, H316, H320, H333,*  
2 *H335, H336, H362, and H400's. These H-codes are either not occupationally relevant, or are not sufficient to effect the Tier 1*  
3 *banding result.*

4 These codes and categories provide a basis to categorize chemicals based on the severity and  
5 reversibility of the health effects. Chemicals that have the potential to cause severe and  
6 irreversible health effects at relatively low doses, such as carcinogens, reproductive toxicants,  
7 acutely fatal compounds, and corrosive materials, are systematically assigned to the most  
8 protective bands. Chemicals that cause reversible health effects at higher doses, such as skin and  
9 eye irritants, are assigned less protective bands, given that the health outcomes are less severe.  
10 As shown in the Tier 1 Overview (Figure 2-1), GHS codes are used to discriminate between  
11 extremely potent chemicals (assigned to bands D or E) and those for which the criteria suggest a  
12 lower level of toxicity. If a chemical has not been evaluated in the GHS system, it cannot be  
13 banded in Tier 1. Additionally, chemicals that have been evaluated by GHS, but have not been  
14 assigned any 300-level H-codes cannot be banded either. These chemicals require a Tier 2  
15 evaluation for band assignment. In general, Tier 1 can be used as a quick screening method, but  
16 NIOSH recommends going to Tier 2 if the user expertise is available. Tier 1 would likely be  
17 more be useful when banding a large number of chemicals and deciding which ones should be  
18 prioritized for elimination or substitution.

## DRAFT

1 Figure 2-1: Tier 1 overview for quickly banding chemicals in Tier 1.  
2



3

### 4 **2.1. GHS Hazard Statements, Codes, and Categories**

5 Hazard statements, codes, and categories are aligned with a standardized hazard criterion for  
6 toxicological endpoints defined by GHS. These endpoints are called *hazard classes*. As  
7 described in the overview, the health hazard classes as defined by GHS comprise (1)  
8 carcinogenicity, (2) reproductive toxicity, (3) specific target organ toxicity, (4) genotoxicity, (5)  
9 respiratory sensitization (6) skin sensitization, (7) acute toxicity, (8) skin corrosion and irritation,  
10 and (9) eye damage/irritation. GHS *hazard statements* are standardized phrases that capture the  
11 nature and extent of the potential risks to human health through contact with a chemical agent. A  
12 given chemical may have a hazard statement for any or each of these endpoints, and the  
13 statements will vary depending on the severity of the endpoint. For example, a range of GHS  
14 health hazard statements address the acute toxicity potentially associated with dermal exposure  
15 to a chemical. These statements include, “May be harmful in contact with skin,” “Harmful in  
16 contact with skin,” “Toxic in contact with skin,” and “Fatal in contact with skin.”

30

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1 Each hazard statement assigned to a chemical by GHS is accompanied by an alphanumerical  
2 hazard code. Marked by simplicity and ease of use, hazard codes related to health endpoints  
3 always begin with the letter H followed by the digit 3. For example, “May be harmful in contact  
4 with skin” is represented by the code H313 and “Fatal in contact with skin” is coded H310.

5 Under GHS, chemicals are also assigned a hazard category. A hazard category is the division of  
6 criteria within each hazard class. These categories compare hazard severity within a hazard class  
7 and are assigned according to specific toxicological cut-points (such as median lethal dose  
8 [LD<sub>50</sub>]) values for acute toxicity) or expert judgement decisions, such as for assessing the  
9 potential for human carcinogenicity. The hazard category can often provide greater distinction  
10 and more specific information than hazard statements and codes.

11 The full suite of GHS hazard codes, statements, hazard categories is listed in Table A3.1.2 of  
12 [UNECE 2013]. As illustrated in Table 2-1 of this document, most of these hazard code and  
13 category combinations correspond to a band in the NIOSH occupational exposure banding  
14 scheme.

### 15 **2.2. Data Sources for Hazard Codes and Categories**

16 A number of resources can be used to obtain hazard statements, codes, and categories. NIOSH  
17 recommends the following as information sources:

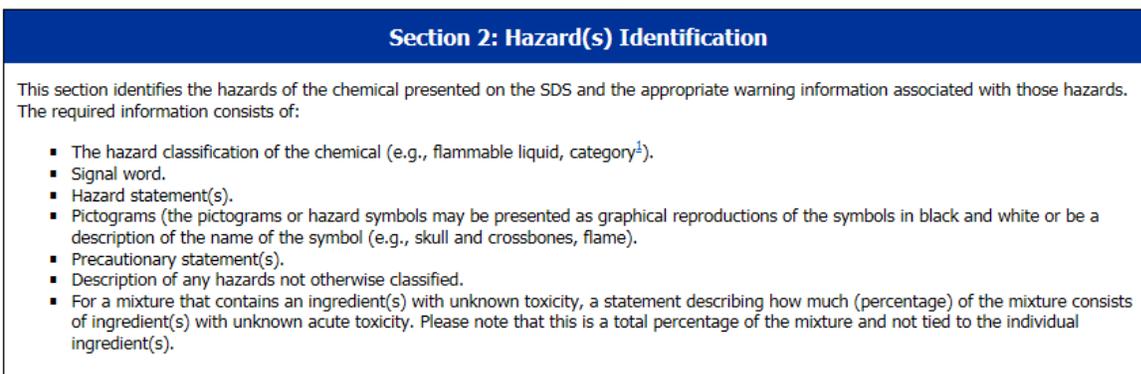
18

#### 19 ***Safety Data Sheets***

20 Safety data sheets (SDSs) are the primary channel through which manufacturers communicate  
21 chemical safety and health information to workers and emergency response personnel who may  
22 be exposed to hazardous chemicals. The OSHA hazard communication standard is now aligned  
23 with the GHS, meaning that manufacturers must provide a harmonized hazard statement for each  
24 hazard class and category [OSHA 2012]. As of June 1, 2015, OSHA-compliant SDSs will  
25 contain GHS hazard statements, codes, and categories that can be used for Tier 1 analysis  
26 (Figure 2-2).

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1 Figure 2-2: Required elements in Section 2 of OSHA compliant safety data sheets as defined by the  
2 hazard communication standard (29 CFR 1910.1200(g)), revised in 2012.



3  
4 **Annex VI to the Classification, Labelling and Packaging of substances and mixtures (CLP)**  
5 Annex VI is a European database of approximately 1300 chemicals that is part of the  
6 Classification and Labeling and Packaging of chemical substances and mixtures. This database  
7 can be found on the website of the European Chemical Agency [ECHA 2013]. Information on  
8 chemicals and mixtures, including GHS hazard statements, codes, and categories can be found in  
9 Annex VI.

10  
11 **GESTIS Substance Database**  
12 GESTIS is a hazardous chemical database of the German Social Accident Insurance that contains  
13 approximately 8000 chemicals [GESTIS 2012]. This website can be found at: [http://gestis-](http://gestis-en.itrust.de/)  
14 [en.itrust.de/](http://gestis-en.itrust.de/). Information in GESTIS includes toxicological data, physical and chemical  
15 properties, regulations, and hazard statements, codes, and categories.

### 16 2.3. Steps in the Tier 1 Analysis

17 The first step in the Tier 1 analysis is to determine whether an authoritative (i.e., government,  
18 consensus, or peer-reviewed) or reliable internal OEL is available for the chemical under  
19 consideration. Examples include, but are not limited to NIOSH recommended exposure limits  
20 (RELs), OSHA permissible exposure limits (PELs), American Conference of Governmental  
21 Industrial Hygienists (ACGIH) threshold limit values (TLVs)<sup>®</sup>, American Industrial Hygiene  
22 Association (AIHA) /Occupational Alliance for Risk Science (OARS) workplace environmental  
23 exposure limits (WEELs), and European Union (EU) scientific committee on occupational  
24 exposure limits. Current OEL information can be found on an OSHA-compliant SDS, in the  
25 NIOSH Pocket Guide for Chemical Hazards [NIOSH 2010], or any updates provided by the  
26 organization that derived the OEL being considered. If one of these OELs is available, it is not  
27 necessary to define an OEB. Controls should be implemented to limit worker exposure to the  
28 available OEL. This step is important as it highlights the fact that OEBs are not a replacement to

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1 a traditional OEL, the latter typically having much greater data requirements and more in-depth  
2 data evaluation and peer review procedures. However, in the absence of existing government,  
3 consensus, or peer-reviewed OELs, occupational exposure banding can be used to make  
4 decisions about worker exposure and protection.

5 In gathering information for Tier 1, the user should identify the hazard codes and categories  
6 assigned to the agent. These can be found in the sources listed in Section 1.3 of this document.  
7 For hazard banding purposes, majority of the 300-level hazard codes are used, as they  
8 correspond to health hazards. Some 300-level codes are not included, as they represent health  
9 effects that are not sufficient for Tier 1 banding. The 300-level hazard codes that are not used  
10 for banding include: H303, H305, H313, H316, H320, H333, H335, H336, and H362.  
11 Furthermore, 200-level hazard codes that correspond to physical hazards and 400-level hazard  
12 codes that correspond to ecotoxicology are also not used for banding purposes.

13 Using the hazard codes assigned to a given chemical for each toxicological endpoint, the  
14 technical criteria listed in Table 2-1 provide guidance on the selection of the corresponding OEB  
15 for that endpoint. The band for each health endpoint for which H codes are available is entered  
16 into the Tier 1 spreadsheet. Where multiple H-codes for a single chemical are found and those H-  
17 codes correspond to different bands, the overall OEB is defined as the most protective band. For  
18 example, if Tier 1 H-codes are found that correspond with band D and band E, the chemical is  
19 assigned band E in Tier 1.

20 To assist the user in completing the Tier 1 banding process, Appendix A contains the Tier 1  
21 criteria along with a blank worksheet that can be used to record H-codes, hazard categories, and  
22 the corresponding endpoint specific band. The most protective of these bands is recorded at the  
23 bottom of the spreadsheet. This is the Tier 1 OEB for the chemical.

24  
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1 **2.4 Detailed Example of a Chemical Banded in Tier 1 (Table 2-2)**

2  
3 **Chloral hydrate (302-17-0)**

- 4
- 5 (1) Select a chemical that you are interested in evaluating.
- 6 a. Chloral hydrate (302-17-0)
- 7
- 8 (2) Determine if an authoritative OEL, such as a NIOSH REL, OSHA PEL, or ACGIH TLV
- 9 is available. If so, implement controls to limit worker exposure to that level. If not,
- 10 proceed with banding process.
- 11 a. No OEL, so proceed to Tier 1 banding.
- 12
- 13 (3) Determine the three-digit H-codes and hazard categories assigned to the chemical by
- 14 GHS. These H-codes and hazard categories can be found in Annex 6 of the GHS, the
- 15 GESTIS database, and updated, OSHA compliant SDSs. *Note: All 300-level H-codes*
- 16 *correspond to a health hazards. Two hundred-level H-codes correspond to physical*
- 17 *hazards, and 400-level correspond to ecotoxicology.*
- 18 a. For chloral hydrate, the H-codes are H315, H319, and H301
- 19 b. The categories are Eye Irrit 2, Skin Irrit 2, and Acute Tox 3
- 20
- 21 (4) Use the Tier 1 criteria overview to determine which OEB corresponds to each of the
- 22 health based (300-level) H-codes for that chemical. Find the H-code on the chart, and
- 23 find the corresponding OEB at the top of the column. If no H-code exists for a particular
- 24 endpoint, that endpoint cannot be banded. Note: When H-codes correspond to more than
- 25 one band, the hazard category is used to determine the endpoint specific band.
- 26
- 27 (5) Assign the overall occupational exposure band for the chemical based on the H-code(s)
- 28 that is/are most protective based on the following rules:
- 29 a. If no H-codes are available for the chemical, do not band in Tier 1. Proceed to
- 30 Tier 2.
- 31 b. The overall band in a Tier 1 process is never less protective than band C.
- 32 c. If the most protective H-code corresponds to both bands D and E, the hazard
- 33 categories should be used to make the final determination. If the hazard category
- 34 is not available, band E should be assigned.

35 For chloral hydrate, the most protective H-codes correspond to **band C**.

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1 **Table 2-2: Tier 1 Example**

<b>Chemical Name: Chloral Hydrate</b>					
<b>CAS: 302-17-0</b>					
<b>Endpoint</b>		<b>Hazard Code</b>	<b>Hazard Category</b>	<b>H-code Source</b>	<b>Endpoint Band</b>
<b>Acute Toxicity</b>	<b>Inhalation</b>				<b>C</b>
	<b>Oral</b>	H301	Category 3	GHS	
	<b>Dermal</b>				
<b>Skin Corrosion/Irritation</b>		H315	Category 2	GHS	<b>C</b>
<b>Serious Eye Damage/ Eye Irritation</b>		H319	Category 2	GHS	<b>C</b>
<b>Respiratory and Skin Sensitization</b>					
<b>Germ Cell Mutagenicity</b>					
<b>Carcinogenicity</b>					
<b>Reproductive Toxicity</b>					
<b>Specific Target Organ Toxicity</b>					
<b>Most Protective Band</b>					<b>C</b>

2

# Chapter 3 : Banding Chemicals beyond GHS: The Tier 2 Occupational Exposure Banding Process

## 3.0. Overview

The Tier 2 process is recommended by NIOSH whenever data allow because it is more precise than Tier 1 and utilizes point of departure data. If the Tier 1 evaluation results in a band E, Tier 2 is optional given that band E represents the lowest exposure concentration range and a Tier 2 process would not result in a more stringent recommendation. However, completing the Tier 2 process could be beneficial even in this situation, as the user may gather more detailed chemical information and possibly move the chemical into a different band. It is most helpful for chemicals for which (1) there are no GHS H-codes/statements through which a Tier 1 analysis can be achieved, or (2) the outcome of the latter analysis is incomplete, uncertain, or newer information is available that more clearly reflects the health potency of the chemical.

The process for Tier 2 occupational exposure banding uses information and data for nine standard toxicological endpoints and/or health outcomes that are readily available from secondary sources such as agency reviews. Endpoints evaluated include acute toxicity, skin corrosion and irritation, serious eye damage and irritation, respiratory sensitization, skin sensitization, genotoxicity, carcinogenicity, reproductive/developmental toxicity, and specific target organ toxicity resulting from repeated exposure (STOT-RE).

Sources of toxicological information have been assessed and assigned as Rank 1 (preferred sources) or Rank 2 (second-level sources). Rank 1 sources are those that are most likely to contain accurate and readily available toxicity data. In the case that information is not found in Rank 1 sources, the user is advised to search Rank 2. It is not necessary to consult Rank 2 if appropriate data are collected from Rank 1. Rank 1 and Rank 2 sources are identified in Table 3-2.

The toxicity information for some of the health effects listed above may be categorical in nature (presence/absence of genotoxicity or skin irritation, for example) while other outcomes are expressed through quantitative information and/or potency data. In the latter case, clearly specified quantitative benchmarks, such as median lethal doses (LD<sub>50</sub>s) for acute toxicity and no-observed-adverse-effect levels (NOAELs), or equivalent point of departure such as benchmark dose lower confidence limit (BMDL), for STOT-RE, are used. Those NOAEL/BMDL values that are used as the basis of agency-derived toxicity benchmarks, such as the reference dose (RfD) from the U.S. Environmental Protection Agency (U.S. EPA) or minimum risk level

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1 (MRL) from the Agency for Toxic Substances and Disease Registry are preferred for assessing  
2 chemicals in Tier 2 (Rank 1 or preferred sources), when possible. (Note: The NOAEL/BMDL  
3 (or, in some cases lowest observed adverse effect level) are used in this analysis, NOT the  
4 agency RfD or MRL, because of differences in purpose and dose adjustments.) In the absence of  
5 preferred NOAEL/BMDL values from such agency authenticated toxicity benchmarks, clearly  
6 documented NOAELs/BMDLs from one or more of a suite of designated information sources  
7 can be used (Rank 2 or second-level sources).

8 The numerical cut points defining each OEB reflect the spectrum of possible outcomes, from  
9 little or no adverse effects (band A) through highly toxic/lethal at low exposures (band E).  
10 Earlier, unpublished versions of the Occupational Exposure Banding process included band-  
11 specific ranges that approximate the GHS hazard categories, but has refined these cut points  
12 based on exposure response analyses, comparisons of OEBs to current OELs, and technical  
13 expertise. To ensure the cut points reflect a range of potencies, the fraction of chemicals covered  
14 by each occupational exposure band was determined and compared to the potency distribution of  
15 a diverse set of chemicals for some endpoints. Additionally, a range of uncertainty factors were  
16 considered for deriving OELs that correspond to each band, including interspecies extrapolation,  
17 human variability, and severity of effects.

18 The Tier 2 process for occupational exposure banding also assesses the sufficiency of toxicity  
19 data to ensure that adequate information is available to reliably band a chemical. When toxicity  
20 data are present for a given endpoint, a weighted score based on that health endpoint is assigned.  
21 The scoring process yields an endpoint determinant score (EDS) for each health end point and a  
22 total determinant score (TDS) which is the sum of the scores based on the presence of data for  
23 each health endpoint. The TDS is compared to a predetermined threshold for data sufficiency  
24 (see Table 3-1). The TDS is an indication of the presence or absence of data. The TDS was  
25 developed using professional judgment with consideration of the severity of health outcomes and  
26 the likelihood that data regarding a particular endpoint would indicate that the chemical is  
27 sufficiently scrutinized to assign a band. It informs the user whether or not there is enough data  
28 to make a banding decision.

29 This document provides an overall strategy for finding the information needed to band a  
30 chemical. Additionally, the process for scoring the availability and sufficiency of data for  
31 banding in Tier 2 is described. Finally, an electronic web tool and paper worksheets are available  
32 for calculating the TDS and determining the OEB.

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1 **Table 3-1: Assigned Scores for the Presence of Toxicological Endpoints Encountered in the Tier 2**  
2 **Evaluation**

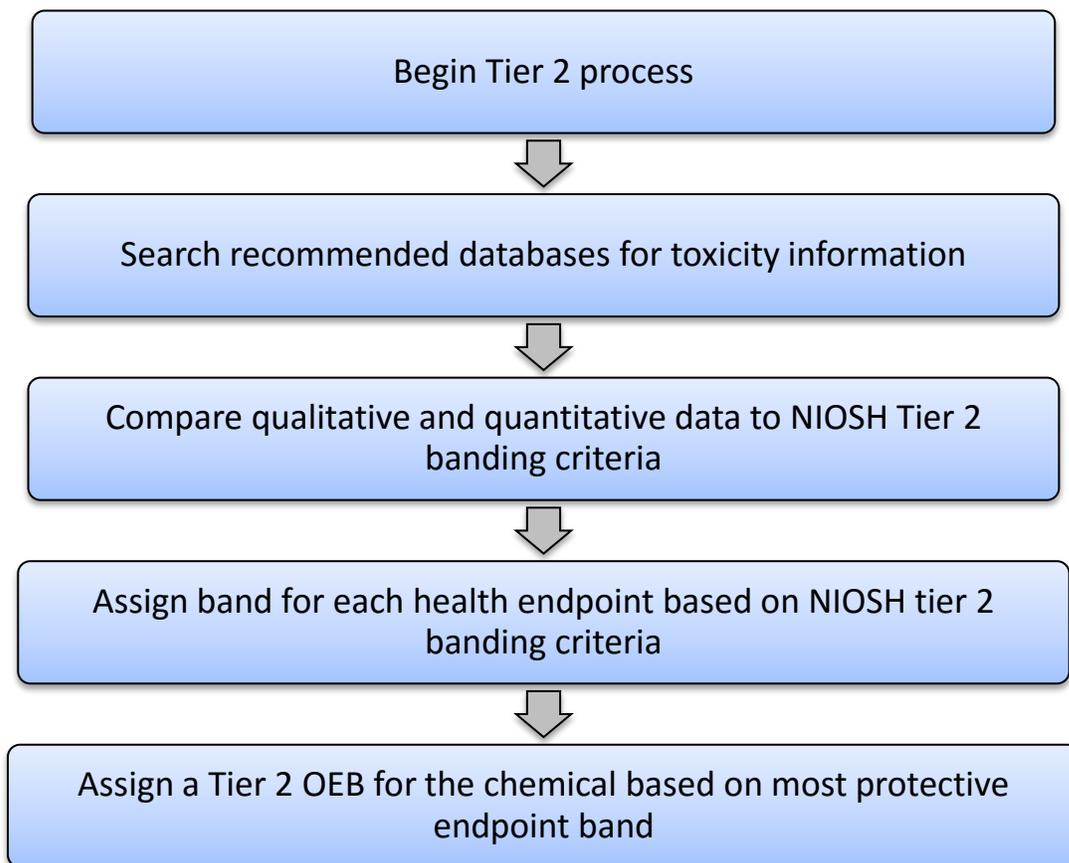
<b>Toxicological Endpoint</b>	<b>Endpoint Determinant Score (EDS)</b>
Skin Irritation/Corrosion	5
Eye Irritation/Corrosion	5
Skin Sensitization	5
Acute Toxicity/Lethality (LD <sub>50</sub> or LC <sub>50</sub> )	5
Genotoxicity	5
Respiratory Sensitization	10
Systemic Target Organ Toxicity (STOT-RE)	30
Reproductive and Developmental Toxicity	30
Cancer WOE	20 or 30
Cancer SF, IUR, or TD/TC <sub>05</sub> (Health Canada)	30
<b>Data Sufficiency/Total Determinant Score (TDS)</b>	30/125

3  
4

### 3.1. Overall Strategy for Banding Chemicals in Tier 2

The overall Tier 2 process involves collecting quantitative and qualitative toxicity information on the nine toxicological endpoints using NIOSH-recommended data sources (Table 3-2). These sources have been assigned as Rank 1 (preferred sources) or Rank 2 (secondary sources). If information is available in Rank 1, it is not necessary to search Rank 2 sources. The sources are also presented in Table 3-3. In Table 3-3 allows the user to quickly identify which endpoints each source may have data for. Data can be recorded electronically via the NIOSH Occupational Exposure Banding eTool or manually via the worksheets located in Appendix B of this document. Endpoint-specific findings are documented in the spreadsheet, and the OEB technical criteria are used to assign endpoint-specific bands and determinant scores for the presence of data. If the TDS is at least 30, indicating that sufficient data are available for banding, the most protective endpoint-specific band is assigned as the OEB. The eTool automatically calculates the TDS, or the TDS can be calculated by the user by adding all of the EDS values together. This process is described in Figure 3-1.

Figure 3-1: Overview of Tier 2 process



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1 **Table 3-2: List of Information Sources for Banding in Tier 2**

2

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
<b>Carcinogenicity</b>	1	U.S. National Toxicology Program Report on Carcinogens [NTP-ROC 2016]	NTP-RoC
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS
		International Agency for Research on Cancer [IARC 2015]	IARC
		Health Canada [Canada 1996]	HC
		State of California Office of Environmental Health Hazard Assessment [CAL/EPA 2010]	Cal OEHHA
<b>Reproductive toxicity</b>	1	U.S. National Toxicology Program [NTP 2016]	NTP
		Health Canada [Canada 1996]	HC
		California Environmental Protection Agency [CAL/EPA 2016]	CalEPA
		Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
	2	Organization for Economic Co-operation and Development [OECD 2016]	OECD
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
		U.S. EPA Office of Pesticides: Reregistration Eligibility Decision Documents [EPA 2016a]	U.S. EPA RED
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	ECHA; REACH
<b>Specific Target Organ Toxicity (STOT-RE)</b>	1	Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS
		California Environmental Protection Agency [CAL/EPA 2016]	CalEPA
		U.S. National Toxicology Program [NTP 2016]	NTP
		Health Canada [Canada 1996]	HC
	2	European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
		Organization for Economic Co-operation and Development [OECD 2016]	OECD
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS

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<b>Genotoxicity</b>	1	U.S. National Toxicology Program [NTP 2016]	NTP
		Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. National Toxicology Program Report on Carcinogens [NTP-ROC 2016]	NTP-RoC
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
	2	Hazardous Substance Data Bank [HSDB 2016]	HSDB
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
<b>Respiratory sensitization</b>	1	Organization for Economic Co-operation and Development [OECD 2016]	OECD
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
	2	Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS
		Association of Occupational and Environmental Clinics [AOEC 2016]	AOEC
<b>Skin sensitization</b>	1	NIOSH Skin Notation Profiles [NIOSH 2009b]	SK Profiles
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
		Organization for Economic Co-operation and Development [OECD 2016]	OECD
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
	2	Hazardous Substance Data Bank [HSDB 2016]	HSDB
<b>Acute Toxicity</b>	1	National Library of Medicine ChemID Plus [ChemID 2016]	ChemID Plus
		U.S. EPA Superfund Chemical Data Matrix [EPA 2016b]	U.S. SCDM
		Pesticide Properties Database [PPDB 2007]	PPDB
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS

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	2	Hazardous Substance Data Bank [HSDB 2016]	HSDB
		Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
<b>Skin Irritation/Skin Corrosion</b>	1	NIOSH Skin Notation Profiles [NIOSH 2009b]	SK Profiles
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
		Organization for Economic Co-operation and Development [OECD 2016]	OECD
	2	Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS
<b>Serious Eye Damage/Eye Irritation</b>	1	Organization for Economic Cooperation and Development [OECD 2016]	OECD
		World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]	WHO-IPCS
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]	REACH
	2	Agency for Toxic Substances & Disease Registry Toxicological Profiles [ATSDR 2016]	ATSDR
		U.S. EPA Integrated Risk Information System [EPA 2014]	IRIS

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1 **Table 3-3: Recommended Sources for Tier 2 Banding by Endpoint**

2

Sources	OEB Endpoint								
	Cancer	Reproductive Toxicity	STOT. RE	Genotoxicity	Respiratory Sensitization	Skin Sensitization	Acute Toxicity	Skin Corrosion/Irritation	Eye Corrosion/Irritation
<b>NTP-ROC</b>	Rank 1			Rank 1					
<b>NTP</b>	Rank 1	Rank 1	Rank 1	Rank 1					
<b>IRIS</b>	Rank 1		Rank 1		Rank 2			Rank 2	Rank 2
<b>IARC</b>	Rank 1								
<b>HC</b>	Rank 1	Rank 1	Rank 1						
<b>Cal OEHHA</b>	Rank 1								
<b>ATSDR</b>		Rank 1	Rank 1	Rank 1	Rank 2		Rank 2	Rank 2	Rank 2
<b>Cal EPA</b>		Rank 1	Rank 1						
<b>OECD</b>		Rank 2	Rank 2		Rank 1	Rank 1		Rank 1	Rank 1
<b>Chem ID plus</b>							Rank 1		
<b>US SCDM</b>							Rank 1		
<b>PPDB</b>							Rank 1		
<b>NIOSH SKN</b>						Rank 1		Rank 1	
<b>HSDB</b>				Rank 2		Rank 2	Rank 2		
<b>AOEC</b>					Rank 2				
<b>WHO-IPCS</b>		Rank 2	Rank 2	Rank 1	Rank 1	Rank 1	Rank 1	Rank 1	Rank 1
<b>REACH</b>		Rank 2		Rank 2	Rank 1	Rank 1		Rank 1	Rank 1
<b>EPA RED</b>		Rank 2	Rank 2						

3

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## 1 **3.2. Assessing Data Sufficiency for Hazard Banding in Tier 2: The Total** 2 **Determinant Score**

3 A compound's TDS is defined as a quantitative measure of data sufficiency for banding in Tier 2  
4 of the evaluation. The TDS is the end product of a scoring system based on the availability of  
5 quantitative and/or categorical (semi-quantitative) information on the entire range of  
6 toxicological outcomes (determinants).

7 A Tier 2 evaluation for banding purposes is potentially more discriminating than that based on  
8 GHS statements and codes, and could result in a chemical being moved from the band selected in  
9 the Tier 1 evaluation. However, assessing the sufficiency of information is desirable in Tier 2 to  
10 avoid overreliance on an inadequate or limited data set that may not reflect the potential health  
11 hazard that occupational exposure to a chemical represents.

12 A numerical scheme for data adequacy is used to evaluate chemicals with different combinations  
13 of toxicological outcomes and available data.

### 14 **Technical Approach**

15 Individual scores are assigned to chemicals for the presence of determinant-specific information.  
16 The individual score for a given health endpoint is referred to as the endpoint determinant score  
17 (EDS). The TDS, which is the sum of the EDS values, is then compared to a predetermined  
18 numerical threshold (30 points). This threshold is a professional judgment on the minimum  
19 amount of information for assigning a chemical to a band in Tier 2 with reasonable reliability.

20 As shown in Table 3-1, different scores are used for the presence of different toxicological  
21 outcomes. These EDS values represent weights for the relative importance and severity of the  
22 toxicological outcomes under consideration. Thus, the presence of cancer and the existence of  
23 quantitative data on systemic toxicological impacts score higher than less severe or life-  
24 threatening outcomes, such as eye irritation. Recognizing this disparity, the scheme assigns an  
25 EDS of 30 to a chemical for the presence of quantitative data or categorical information on  
26 cancer and a score of 30 for systemic toxicity to target organs such as the liver or kidney, etc. In  
27 contrast, a score of 5 is assigned for toxicological outcomes that are either less crucial to the  
28 overall health of an exposed individual or less reliable as an index of chemical hazard through  
29 occupational exposure (for example, acute toxicity).

30 As shown in Table 3-1, the data sufficiency threshold of 30 (out of a maximum possible TDS of  
31 125) has been selected empirically with the goal of ensuring that at least one of the more health  
32 critical endpoints is present for a chemical to be banded in Tier 2. A chemical-specific TDS of  
33 less than 30 would indicate that the substance cannot be reliably banded in Tier 2. In such  
34 circumstances, a Tier 3 evaluation would be necessary. A TDS of 30 or more would justify

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1 choosing the most stringent band from all of the determinants evaluated as the Tier 2 outcome. If  
2 this differs from the outcome of the Tier 1 evaluation, it would then be justifiable to band the  
3 chemical to either a less or more health protective band than that obtained in Tier 1. The  
4 minimum TDS criteria are waived if any of the endpoint bands are E. In this case, the chemical is  
5 assigned an overall band E regardless of TDS. The rationale for this is that even when very  
6 limited data are available, indications of high toxicity should alert the user to adopt the most  
7 stringent band until additional toxicity data are generated.

### 8 **Practical Considerations: The Endpoint Determinant Score**

9 The concept of an EDS has been introduced to avoid overreliance on a particular determinant for  
10 banding where several data points may be available within a specific toxicological category.  
11 Thus, if a number of indices of acute toxicity are available (LD<sub>50</sub>, LC<sub>50</sub>) for a particular  
12 chemical, simplistically, these might unbalance the evaluation by resulting in an EDS of 10.  
13 However, using the EDS concept, the presence of any or all of these determinants would still  
14 result in an EDS of 5. The Tier 2 checklist shows how this information should be recorded (see  
15 highlighted cells in Table 3-4).

### 16 **Special TDS considerations for Cancer Data**

17 If quantitative cancer information for a chemical is available, it will take precedence over  
18 qualitative or categorical data. An EDS of 30 is assigned for any type of quantitative data  
19 described in the NIOSH criteria (e.g. SF, TD<sub>05</sub>, TC<sub>05</sub>, etc.). In the absence of quantitative data,  
20 categorical data is used. An EDS of 20 is assigned for the presence of categorical data, **except**  
21 when the categorical data results in a band E. In the latter case, an EDS of 30 is assigned.

**DRAFT**

1 **Table 3-4: Checklist for Tier 2 Hazard Banding**

<b>Chemical Name:</b>			
<b>CAS:</b>			
<b>Endpoint</b>	<b>Data</b>	<b>EDS</b>	<b>Endpoint Band</b>
<b>Acute Toxicity</b>	Source:		
<b>Skin Corrosion/Irritation</b>	Source:		
<b>Serious Eye Damage/ Eye Irritation</b>	Source:		
<b>Respiratory Sensitization</b>	Source:		
<b>Skin Sensitization</b>	Source:		
<b>Genotoxicity</b>	Source:		
<b>Carcinogenicity</b>	Source:		
<b>Reproductive Toxicity</b>	Source:		
<b>Specific Target Organ Toxicity</b>	Source:		
<b>OVERALL Tier 2 BAND</b>		<b>TDS=</b>	

**3.3. Banding Potentially Hazardous Chemicals on the Basis of Carcinogenicity**

Cancer is a group of diseases that cause cells in the body to change and grow out of control. Abnormally reproducing cells of this kind can spread throughout the body (metastasize), crowding out normal cells and tissue in the process [ACS 2013].

A *carcinogen* is a “. . . substance or a mixture of substances which induce cancer or increase its incidence. Substances which have induced benign and malignant tumors in well performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumor formation is not relevant for humans. . . More explicitly, chemicals are defined as carcinogenic if they induce tumors, increase tumor incidence and/or malignancy or shorten the time to tumor occurrence. Benign tumors that are considered to have the potential to progress to malignant tumors are generally considered along with malignant tumors. Chemicals can potentially induce cancer by any route of exposure (e.g., when inhaled, ingested, applied to the skin, or injected), but carcinogenic potential and potency may depend on the conditions of exposure (e.g., route, level, pattern and duration of exposure).” [UNECE 2013]

Evidence of an agent’s carcinogenic potential in humans may arise from studies of groups of people who have been exposed environmentally or in the workplace or from long-term studies in experimental animals.

**Data Sources – Carcinogenicity**

Sources for Tier 2 information for carcinogenicity can be found in Table 3-5.

**Table 3-5: Information Sources for Carcinogenicity Endpoint**

<b>ENDPOINT</b>	<b>Rank</b>	<b>SOURCE OF INFORMATION</b>	<b>ACRONYM</b>
<b>Carcinogenicity</b>	1	U.S. National Toxicology Program Report on Carcinogens	NTP-RoC
		U.S. EPA Integrated Risk Information System	IRIS
		International Agency for Research on Cancer	IARC
		Health Canada	HC
		State of California Office of Environmental Health Hazard Assessment	Cal OEHHA

**Classification Criteria – Carcinogenicity**

Carcinogenicity can be assessed quantitatively or qualitatively, depending on the data available. For banding purposes, either qualitative assessments or quantitative assessments can be used, but if both are available, the banding resulting from the quantitative assessment takes precedence. Recommended sources for information about carcinogenicity are listed in Table 3-5.

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### 1 Quantitative Assessment – Carcinogenicity

2 The quantitative assessment of carcinogenicity uses a measure of potency as a more accurate  
3 way to band chemicals than a purely qualitative approach. Because OEBs represent  
4 concentration ranges, potency information is more valuable in terms of selecting the appropriate  
5 band. Potency data, when available, may be in the form of a slope factor (SF), an inhalation unit  
6 risk (IUR), or a tumorigenic dose (TD<sub>05</sub>) or concentration (TC<sub>05</sub>) associated with a 5% increase  
7 in tumor incidence or mortality. To conduct a quantitative assessment, the potency measure is  
8 converted to appropriate units (if necessary) and compared to quantitative banding criteria to  
9 select the appropriate band shown in Table 3-6.

10 **Table 3-6: Criteria for Carcinogenicity Toxicity (Quantitative Analysis)**

NIOSH Banding Criteria for <b>Cancer</b>			
Exposure/ Dosing Route	Endpoint Band		
	C	D	E
Slope factor	$< 0.01 \text{ (mg/kg-day)}^{-1}$	$\geq 0.01 \text{ to } < 10 \text{ (mg/kg-day)}^{-1}$	$\geq 10 \text{ (mg/kg-day)}^{-1}$
Inhalation unit risk	$< 3 \times 10^{-6} \text{ (}\mu\text{g/m}^3\text{)}^{-1}$	$\geq 3 \times 10^{-6} \text{ to } < 0.01 \text{ (}\mu\text{g/m}^3\text{)}^{-1}$	$\geq 0.01 \text{ (}\mu\text{g/m}^3\text{)}^{-1}$
TD <sub>05</sub>	$> 5 \text{ mg/kg-day}$	$> 0.005 \text{ to } \leq 5 \text{ mg/kg-day}$	$\leq 0.005 \text{ mg/kg-day}$
TC <sub>05</sub>	$> 16700 \text{ }\mu\text{g/m}^3$	$> 5 \text{ to } \leq 16700 \text{ }\mu\text{g/m}^3$	$\leq 5 \text{ }\mu\text{g/m}^3$

11  
12 Three sources, U.S. EPA IRIS, Health Canada, and State of California Office of Environmental  
13 Health Hazard Assessment Cal-OEHHA, have sufficient quantitative information to refine the  
14 carcinogenicity hazard band and should be used for quantitative assessment. Once a band has  
15 been selected based on a potency estimate, there is no need to go on to the next source for this  
16 analysis.

### 17 Endpoint-Specific Band Selection – Quantitative Carcinogenicity

- 18 • To band a chemical using an SF or IUR, first ensure that the values are in the appropriate  
19 units or convert the values to the appropriate units.
  - 20 • Compare the SF or IUR to the quantitative criteria and assign a band accordingly. (Table  
21 3-6). The band assigned on the basis of SF or IUR takes precedence over any band  
22 assigned based on a qualitative description.
  - 23 • If both a SF and an IUR are available, whichever gives the more protective band takes  
24 precedence for band selection in Tier 2. The most protective SF and IUR values are the  
25 highest, rather than the lowest values, as these values represent the proportion of a  
26 population at risk for developing cancer.
  - 27 • If a TD<sub>05</sub> is available for the agent, ensure that the units are mg/kg-day.
  - 28 • If a TC<sub>05</sub> is available for the agent, ensure that the units are  $\mu\text{g/m}^3$ .
  - 29 • If quantitative carcinogenicity data are available, assign a EDS of 30 points.
- 30

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### 1 **Qualitative Assessment – Carcinogenicity**

2 In the qualitative assessment, sources in Table 3-2 should be checked for carcinogen  
3 classifications and assessed using criteria in Table 3-7. Special guidance for each of these  
4 sources follows.

5 **Table 3-7: Criteria for Carcinogenicity Toxicity (Qualitative Analysis)**

Classification	Endpoint Band	Endpoint Determinant Score
<b>National Toxicology Program Report on Carcinogens</b>		
<i>Known to be human carcinogen</i>	E	30
<i>Reasonably anticipated to be human carcinogen</i>	E	30
<b>Environmental Protection Agency Integrated Risk Information System</b>		
<i>Group A (human carcinogen)</i>	E	30
<i>Carcinogenic to humans</i>	E	30
<i>Group B1 (probable human carcinogen)</i>	E	30
<i>Group B2 (probable human carcinogen)</i>	E	30
<i>Likely to be carcinogenic to humans</i>	E	30
<i>Group C (possible human carcinogen)</i>	D	20
<i>Suggestive evidence of carcinogenic potential</i>	D	20
<i>Group D (not classifiable as to human carcinogenicity)</i>	No band	0
<i>Data are inadequate for an assessment of carcinogenic potential</i>	No band	0
<i>Group E (evidence of non-carcinogenicity for humans)</i>	A	30
<i>Not likely to be carcinogenic to humans</i>	A	30
<b>International Agency for Research on Cancer</b>		
<i>Group 1 (carcinogenic to humans)</i>	E	30
<i>Group 2A (probably carcinogenic to humans)</i>	E	30
<i>Group 2B (possibly carcinogenic to humans)</i>	E	30
<i>Group 3 (not classifiable as to its carcinogenicity to humans)</i>	No band	0
<i>Group 4 (probably not carcinogenic to humans)</i>	A	30
<b>State of California Office of Environmental Health Hazard Assessment</b>		
<i>Type of toxicity = cancer</i>	E	30

6

### 7 **Endpoint-Specific Band Selection - Qualitative Carcinogenicity**

#### 8 **National Toxicology Program Report on Carcinogens**

- 9
- 10 • The most recent Report on Carcinogens (RoC) can be searched for the chemical of  
11 interest. If NTP has classified the chemical as either *known to be human carcinogen* or  
*reasonably anticipated to be human carcinogen*, assign an EDS of 30 and band E.
  - 12 • If neither of these designations is located, this source does not have information about the  
13 carcinogenicity of this chemical. In this case, the EDS is 0. No band is assigned, and the  
14 next source is assessed.

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### 1 Environmental Protection Agency Integrated Risk Information System

- 2 • The U.S. EPA IRIS carcinogen classification can be checked on the U.S. EPA IRIS  
3 website. The weight of evidence (WOE) descriptor should be evaluated.
- 4 • If the WOE descriptor is:
  - 5 ○ *Group A (human carcinogen), Carcinogenic to humans, Group B1 (probable*  
6 *human carcinogen), Likely to be carcinogenic to humans or Group B2 (probable*  
7 *human carcinogen)*, assign a determinant score of 30 and band E.
  - 8 ○ *Group C (possible human carcinogen or suggestive evidence of carcinogenic*  
9 *potential)*, assign a determinant score of 20 and band D. For this group, U.S. EPA  
10 found some evidence of carcinogenicity but the data were not sufficiently robust  
11 to have high confidence in the assessment.
  - 12 ○ *Group D (not classifiable as to human carcinogenicity or data are inadequate for*  
13 *an assessment of carcinogenic potential)*, a determinant score of 0 is assigned. No  
14 band is assigned based on this source. For this group, the EPA did not find  
15 enough information to assess the carcinogenicity of the chemical.
  - 16 ○ *Group E (evidence of non-carcinogenicity for humans or not likely to be*  
17 *carcinogenic to humans)*, assign a determinant score of 30 and endpoint band A.  
18 For this group, EPA found that the data were sufficiently robust to conclude that  
19 the chemical is not likely a human carcinogen.

### 20 International Agency for Research on Cancer

- 21 • The IARC carcinogen classification can be found on the IARC Monograph website  
22 (Table 3-5). Check the corresponding IARC monograph website for any additional  
23 information. If IARC has classified the chemical as
  - 24 ○ Group 1 (carcinogenic to humans), Group 2A (probably carcinogenic to humans)  
25 or Group 2B (possibly carcinogenic to humans), assign a determinant score of 30  
26 and a preliminary endpoint band E.
  - 27 ○ *Group 3 (not classifiable as to its carcinogenicity to humans)* or IARC has not  
28 classified the chemical at all, move to the next source. No score is assigned.
  - 29 ○ *Group 4 (probably not carcinogenic to humans)*, assign a determinant score of 30  
30 and endpoint band A.

### 31 State of California Office of Environmental Health Hazard Assessment

- 32 • CalOEHHA lists chemicals known to cause cancer as part of its Proposition 65 list. The  
33 list is available online and can be searched by name or CAS number? If the chemical has  
34 the designation “cancer” under the heading *Type of Toxicity*, assign a determinant score  
35 of 30 and endpoint band E.

### 36 Health Canada

- 37 • Health Canada does not independently assess carcinogenicity with WOE descriptors.  
38 Instead, they report carcinogenicity designations from ACGIH, CalEPA, the European  
39 Union, IARC, and NTP. This source should not be consulted for qualitative data. Use this  
40 source for quantitative carcinogenicity information only.

41

50

*This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by the National Institute for Occupational Safety and Health. It does not represent and should not be construed to represent any agency determination or policy.*

1 **3.4. Banding Potentially Hazardous Chemicals based on Reproductive Toxicity**

2 Reproductive toxicity includes adverse effects on reproductive health in adults and  
3 developmental toxicity in offspring. As discussed in the NTP monograph *Specifications for the*  
4 *Conduct of Studies to Evaluate the Reproductive and Developmental Toxicity of Chemical,*  
5 *Biological and Physical Agents in Laboratory Animals for the National Toxicology Program*  
6 [NTP 2011], data derived from developmental and reproductive studies focus on three main  
7 topics: (1) fertility and reproductive performance, (2) prenatal development, and (3) postnatal  
8 development.

9 Endpoints of reproductive toxicity include dose-related impacts on fertility and fecundity, and  
10 any changes to interrelated reproductive parameters that may suggest an agent-related  
11 perturbation of reproductive function. These could include effects on estrous cyclicity, sperm  
12 parameters, litter observations, histopathology of reproductive organs at term, and reproductive  
13 indices and performance. Indicators in the latter category might include compound-related  
14 changes to the weights of uterus and placenta, and differences in the numbers of corpora lutea,  
15 implantations, resorptions, and dead and living fetuses.

16 For developmental toxicity, indicators of compound-related impacts to the fetus would be sex  
17 ratio; fetal weight and overall size; incidence of external, visceral, or skeletal malformations or  
18 variations; clinical signs; and/or other fetal changes that become evident on necropsy and  
19 histopathology.

20 Reproductive toxicity includes “adverse effects on sexual function and fertility in adult males  
21 and females, as well as developmental toxicity in the offspring” [UNECE 2013].

22 **Data Sources – Reproductive Toxicity**

23 Sources for Tier 2 information for reproductive toxicity can be found in  
24  
25  
26

27 Table 3-8. Standard animal studies in rats and other experimental animals provide relevant data  
28 for banding chemicals according to reproductive toxicity. In assigning a band for these effects,  
29 NOAELs/BMDLs that are specified in reviews of studies featuring oral, dermal, and inhalation  
30 exposures in experimental animals are aligned to the quantitative technical criteria listed in Table  
31 3-9, with emphasis on those studies conducted using internationally accepted protocols (i.e.,  
32 OECD and U.S. EPA Test Guidelines).

1  
2  
3 **Table 3-8: Sources of Information for Reproductive Toxicity Endpoint**

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Reproductive toxicity	1	U.S. National Toxicology Program	NTP
		Health Canada	HC
		California Environmental Protection Agency	CalEPA
		Agency for Toxic Substances & Disease Registry Toxicological Profiles	ATSDR
	2	Organization for Economic Co-operation and Development	OECD
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
		U.S. EPA Office of Pesticides: Reregistration Eligibility Decision Documents	U.S. EPA RED
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	ECHA; REACH

4  
5 **Classification Criteria – Reproductive Toxicity**

6 For a Tier 2 assessment, human or animal data are needed for assigning a band that reflects the  
7 reproductive toxicity potential of a chemical. NIOSH recommends occupational exposure  
8 banding assignments for reproductive toxicity based on NOAELs/BMDLs (Table 3-9). This  
9 dose-response information provides the quantitative basis for assigning a band for this endpoint.  
10 NOAELs/BMDLs are generally available from reviews conducted by governmental, national,  
11 international, and professional agencies. The dose-response information provides the quantitative  
12 basis for assigning the band for this endpoint.

13 NOAEL and BMDL values should be derived from studies that use internationally accepted test  
14 methods, such as the OECD Guidelines for the Testing of Chemicals and EPA Good Laboratory  
15 Practices (GLP) that assess:

- 16 (1) Developmental toxicity  
17 (2) Perinatal and postnatal toxicity  
18 (3) One-generation or two-generation toxicity  
19 (4) Reproductive/developmental toxicity  
20 (5) Combined repeated dose toxicity study with reproduction/developmental toxicity  
21 (6) Short-term or long-term repeated dose toxicity (i.e., studies that have reported adverse  
22 effects or changes that have been judged likely to impair reproductive function and that  
23 occur in the absence of significant generalized toxicity)  
24  
25  
26

1  
2  
3**Table 3-9: Criteria for Reproductive Toxicity Endpoint**

NIOSH Banding Criteria for <b>Reproductive Toxicity</b> (NOAEL/BMDL/BMCL)					
Exposure/ Dosing Route	Endpoint Band				
	A	B	C	D	E
Oral, dermal	> 300 mg/kg-day	> 30 to ≤300 mg/kg-day	> 3 to ≤30 mg/kg-day	> 0.3 to ≤3 mg/kg-day	≤0.3 mg/kg-day
Inhalation (gases and vapors)	> 10,000 ppm	> 1,000 to ≤10,000 ppm	> 100 to ≤1,000 ppm	> 10 to ≤100 ppm	≤10 ppm
Inhalation (dusts and mists)	> 10,000 µg/m <sup>3</sup>	> 1,000 to ≤10,000 µg/m <sup>3</sup>	> 100 to ≤1,000 µg/m <sup>3</sup>	> 10 to ≤100 µg/m <sup>3</sup>	≤10 µg/m <sup>3</sup>

**4 Approach to Data Selection – Reproductive Toxicity**

5 Recommended sources are consulted for relevant NOAELs/BMDLs and, when these are not  
6 available, the LOAEL for the reproductive toxicity endpoint (see Table 3-8 for data sources).  
7 The following approach is suggested.

**8 Endpoint-Specific Band Selection – Reproductive Toxicity**

9 The following steps are suggested to assign a band:

- 10 (1) If route-specific NOAELs/BMDLs are available, use them directly to assign a band.
- 11 (2) If a LOAEL but no NOAEL is available for any route, divide the LOAEL by 10 to  
12 convert the LOAEL to a NOAEL equivalent.
- 13 (3) If multiple NOAELs/BMDLs are available for a given route of exposure, the lowest  
14 NOAEL/BMDL is used for that route.
- 15 (4) When NOAELs/BMDLs are available for multiple exposure routes, assign the most  
16 stringent band as the overall band for the reproductive toxicity of the chemical.
- 17 (5) If no route-specific NOAELs/BMDLs (or LOAELs) are available, criteria for the  
18 reproductive toxicity endpoint are not met and no reproductive toxicity-specific band is  
19 assigned for this chemical.

**20 Endpoint Determinant Score – Reproductive Toxicity**

21 The determination of the availability of adequate data in authoritative reviews to support banding  
22 decisions is based on (1) quantitative epidemiological information on the reproductive effects of  
23 toxicants in exposed humans and/or (2) experimental data on these outcomes in experimental  
24 animals. If a NOAEL/BMDL or LOAEL is available, an EDS of 30 is assigned to indicate  
25 sufficient information is available for banding in Tier 2. This score is assigned on the availability  
26 of the information, regardless of the outcome of the test or observation (positive/negative).

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### 1 **Unit Conversions for Inhalation Data – Reproductive Toxicity**

2 The U.S. EPA [Jarabek et al. 1994] provides a detailed explanation of how the tenets of the ideal  
3 gas law can be used to convert concentrations of gases and vapors expressed in ppm to mg/m<sup>3</sup>  
4 and vice versa.

5 At 25°C and 760 mm Hg 1 g-mole of a perfect gas or vapor occupies 24.45 L; under these  
6 conditions, the conversion becomes:

$$7 \quad \text{mg/m}^3 = (\text{ppm} \times \text{MW})/24.45$$

8 Converting concentrations expressed in mg/m<sup>3</sup> to ppm would require inverting the above  
9 calculation as follows:

$$10 \quad \text{ppm} = (\text{mg/m}^3 \times 24.45)/\text{MW}$$

**3.5. Banding Potentially Hazardous Chemicals on the Basis of Specific Target Organ Toxicity (STOT-RE)**

Specific Target Organ Toxicity following Repeated Exposure (STOT-RE) is the consequence of a “consistent and identifiable toxic effect in humans, or, in experimental animals, toxicologically significant changes which have affected the function or morphology of a tissue/organ, or has produced serious changes to the biochemistry or hematology of the organism and these changes are relevant to human health” [UNECE 2013].

Examples of toxicological endpoints applicable to the STOT-RE hazard banding category include (1) irreversible gross or histopathological changes to major target organs such as the liver and kidney, (2) dose-related trends in absolute or relative organ weights, (3) consistent changes to hematological parameters, and (4) persistent alterations in those clinical chemistry parameters that reflect physiological impairment to one or more target organs. Items in the latter category might include elevations in the serum concentrations of urea nitrogen or creatinine (indicative of damage to the kidneys) or increases in the activities of those enzymes (such as alanine aminotransferase, aspartate aminotransferase, or gamma glutamyl transferase) that are thought to reflect the functional activity of the liver.

**Data Sources – STOT-RE**

Sources for Tier 2 information for STOT-RE can be found in Table 3-10.

**Table 3-10: Criteria for Specific Target Organ Toxicity (STOT-RE) Endpoint**

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Specific Target Organ Toxicity (STOT-RE)	1	Agency for Toxic Substances & Disease Registry Toxicological Profiles	ATSDR
		U.S. EPA Integrated Risk Information System	IRIS
		California Environmental Protection Agency	CalEPA
		U.S. National Toxicology Program	NTP
		Health Canada	HC
	2	European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
		Organization for Economic Co-operation and Development	OECD
		World Health Organization International Programme on Chemical Safety	WHO-IPCS

**Classification Criteria – STOT-RE**

For a Tier 2 assessment, human or animal data are needed for assigning a STOT-RE band to a chemical. These data are generally available from authoritative reviews conducted by governmental, national, international and professional agencies throughout the world. These agencies have published reference doses or concentrations (RfDs and RfCs), minimal risk levels

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1 (MRLs), acceptable daily intakes, tolerable daily intakes or concentrations (TDIs or TDCs),  
2 tolerable intakes (TIs) or tolerable concentrations (TC), etc. These values are based on target  
3 organ toxicity information and criteria specific to the organization that developed them. These  
4 reference doses/concentrations are derived based on NOAELs/BMDLs or LOAELs (when  
5 NOAELs are not available) that are relevant for the STOT-RE classification. The  
6 NOAELs/BMDLs used by the agency to derive the agency recommendations should be used as  
7 the quantitative basis for assigning the band for this endpoint. If the reference dose is based on  
8 something other than STOT-RE (for instance, reproductive toxicity), the NOAEL/BMDL or  
9 LOAEL used to derive the reference dose should not be used for banding for the STOT-RE  
10 endpoint. Instead, those data should be used for the relevant health endpoint.

11 NIOSH recommends criteria for each of the occupational exposure bands as listed in Table 3-11.  
12 The criteria refer to dose/concentrations from standard 90-day toxicity studies conducted in rats.  
13 However, availability of a reliable NOAEL/BMDL from a repeat dose study of adequate quality  
14 in another animal model would be acceptable to assign a STOT-RE band to a chemical.  
15 Similarly, a NOAEL/BMDL from a study of less than 90 days duration (but at least 28 days or)  
16 would be applicable for banding according to this endpoint, if a suitable conversion factor is  
17 applied to account for the shorter duration.

18 **Table 3-11: Criteria for Specific Target Organ Toxicity (STOT-RE) Endpoint**

NIOSH Banding Criteria for <b>Specific Target Organ Toxicity</b> (NOAEL/BMDL)					
Exposure/ Dosing Route	Endpoint Band				
	A	B	C	D	E
Oral, dermal	>1,000 mg/kg-day	>100 to ≤1,000 mg/kg-day	>10 to ≤100 mg/kg-day	>1 to ≤10 mg/kg-day	≤1 mg/kg-day
Inhalation (dusts and mists)	>30,000 µg/m <sup>3</sup>	>3,000 to ≤30,000 µg/m <sup>3</sup>	>300 to ≤3,000 µg/m <sup>3</sup>	>30 to ≤300 µg/m <sup>3</sup>	≤30 µg/m <sup>3</sup>
Inhalation (gases and vapors)	>30,000 ppm	>3,000 to ≤30,000 ppm	>300 to ≤3,000 ppm	>30 to ≤300 ppm	≤30 ppm

19 \* Multiple NOAELs/BMDLs for one chemical may be available. The point of departure value selected for banding should be the  
20 NOAEL/BMDL used by the agency as the basis for the reference dose/concentration.

### 21 **Approach to Data Selection – STOT-RE**

22 When dose-response information and derived target organ toxicity benchmark values are  
23 available from Rank1 sources (Table 2.8), identify, for each route, the single NOAEL/BMDL  
24 that is the most health-protective and enter the value(s) in the appropriate section of the  
25 chemical-specific eTool or paper worksheets. The applicable NOAEL/BMDL is compared to the  
26 NIOSH criteria (Table 3-11).and the most stringent band is assigned as the endpoint band for the  
27 chemical.

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1 In the absence of Rank 1 data, there are other sources of STOT-RE information (e.g.,  
2 authoritative compilation of studies such as SIDS, REACH) from which endpoint-specific  
3 NOAELs/BMDLs may be obtained (Rank 2).

### 4 **Endpoint-Specific Band Selection – STOT-RE**

5 Human data from repeated exposures are the primary source of evidence for this hazard class and  
6 the associated bands, but standard animal studies in rats and other experimental animals that  
7 provide this information are 28-day, 90-day, or lifetime studies (up to 2 years). Because human  
8 data are not readily available, NOAELs/BMDLs are identified in experimental animals following  
9 oral, dermal, and inhalation exposures.

10  
11 Several adjustments may be needed before using data to assign a band. Depending on study  
12 design, a duration-adjustment may be necessary. If 90-day or longer duration NOAELs/BMDLs  
13 are available, these values are used directly to assign a band for a chemical. If a NOAEL/BMDL  
14 is from a 28-day but less than 90-day exposure, this should be divided by a factor of three to  
15 derive a NOAEL/BMDL equivalent to a 90-day exposure. The resulting value is used to assign a  
16 band.

17 Another adjustment that may be required is a LOAEL-to-NOAEL adjustment. If a LOAEL rather  
18 than a NOAEL is available, the LOAEL is divided by 10 to convert the LOAEL to a NOAEL  
19 equivalent.

20 If multiple NOAELs/BMDLs are available for any route of exposure, the lowest value is used for  
21 that route. When NOAELs are available for each route and route-specific bands are assigned, the  
22 overall STOT-RE band is represented by the most health-protective band (the most stringent). If  
23 no route-specific NOAELs are available, criteria for the STOT-RE endpoint are not met and no  
24 STOT-RE specific band will be assigned for this chemical.

### 25 **Endpoint Determinant Score – STOT-RE**

26 The NOAEL/BMDL that serves as the basis for the safe dose/concentration provided in  
27 authoritative reviews can be based on (1) quantitative epidemiological information on STOT-RE  
28 endpoint in exposed humans and/or (2) experimental data on these outcomes in experimental  
29 animals. If a NOAEL/BMDL is available, an EDS of 30 is assigned, indicating sufficient  
30 information is available for banding a chemical in Tier 2.

**3.6. Banding Potentially Hazardous Chemicals on the Basis of Genotoxicity**

The genotoxicity health endpoint is related to changes in genetic material. While genotoxicity and germ cell mutagenicity are similar terms, it is important to draw the distinction. Germ cell mutagens are chemicals that may cause permanent heritable changes in the amount or structure of the genetic material in a germ cell. Germ cells include an ovum or sperm cell or one of its developmental precursors. Mutagenicity refers specifically to heritable changes in the DNA coding sequence, while genotoxicity is a more general term that includes mutations and other DNA or chromosome level changes. Thus, genotoxicity, by definition, includes mutagenicity. Chemicals can be classified as to genotoxicity from a range of in vivo and in vitro tests [UNECE 2013].

Agents with demonstrable genotoxic properties have been subdivided into categories according to the available evidence. For example, chemicals for which positive evidence exists from human epidemiological studies may be regarded as agents *known* to be genotoxic.

In practice, data for few if any genotoxic chemicals rise to this level of certainty, and results from a variety of alternative assays must be considered (see Table 3-12). The process of reaching conclusions regarding genotoxicity potential is challenging because the many different types of assays do not all measure the same aspects of alterations in genetic material. For example, a chemical that causes small changes in the DNA sequence at a single point may not show any effect in assays that primarily assess chromosome changes or large scale DNA damage. Thus, the assessment of genotoxicity potential needs to consider both the nature of available assays as well as the results (positive or negative) for each assay.

**Table 3-12: Examples of Genotoxicity Tests Applicable to the Tier 2 Hazard Banding Process**

Type of test	Examples
In vivo heritable germ cell mutagenicity tests	Rodent dominant lethal mutation test Mouse heritable translocation assay Mouse specific locus test
In vivo somatic cell mutagenicity tests	Mammalian bone marrow chromosome aberration test Mammalian erythrocyte micronucleus test
Mutagenicity tests on germ cells	Mammalian spermatogonial chromosome aberration test Spermatid micronucleus assay
Genotoxicity tests in germ cells	Sister chromatid exchange analysis in spermatogonia Unscheduled DNA synthesis test in testicular cells
Genotoxicity tests in somatic cells	Liver unscheduled DNA synthesis test in vivo Mammalian bone marrow sister chromatid exchange
In vitro mutagenicity tests	In vitro mammalian chromosome aberration test In vitro mammalian cell gene mutation test Bacterial reverse mutation (Ames) test

Source: [UNECE 2013].

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### 1 Approach to Data Selection – Genotoxicity

2 For Tier 2 assessments, the preference is to rely on the overall judgment on genotoxicity  
3 provided from an authoritative Rank 1 or Rank 2 source (Table 3-13). Relevant information on  
4 all of these tests can be found in authoritative reviews and summaries, as listed below. For ease  
5 of access, agent-specific findings are usually gathered together in the relevant section or chapter  
6 and frequently tabulated. Where such authoritative sources are not available, data gathering for  
7 banding chemicals according to this criterion involves searching for chemical-specific data from  
8 a range of genotoxicity tests.

### 9 Data Sources – Genotoxicity

10 Sources for Tier 2 information for Genotoxicity can be found in Table 3-13.

11 **Table 3-13: Sources for Genotoxicity Endpoint**

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Genotoxicity	1	U.S. National Toxicology Program	NTP
		Agency for Toxic Substances & Disease Registry	ATSDR
		U.S. National Toxicology Program Report on Carcinogens	NTP-RoC
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
	2	Hazardous Substance Data Bank	HSDB
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH

### 12 Endpoint-Specific Band Selection - Genotoxicity

13 The totality of the evidence of genotoxicity, as provided by summaries and or tabulated data in  
14 authoritative reviews, should be entered by source in the spreadsheet. If there was no record for a  
15 particular compound enter “no source info.” If there was a record, but no genotoxicity  
16 information enter “no data” for that particular source. If information was found, enter positive or  
17 negative in the appropriate row for that source, depending on the preponderance of the evidence.

18 For the checklist, choose the band that is most appropriate based on the summary statements in  
19 authoritative reviews or evaluation of the data. As shown in Table 3-14, the following bands  
20 apply: A (negative results), C (mixed results), or E (positive results). These determinations are  
21 general in nature, and for data sets that do not provide a clear conclusion regarding genotoxicity  
22 potential a Tier 3 evaluation performed by a toxicologist or other specialist should be considered.  
23 The following are some characteristics of data sets that provide the user the greatest confidence  
24 in the determination of genotoxicity:

- 25 • Availability of a summary statement on genotoxicity from an authoritative source
- 26 • Availability of genotoxicity from in vivo assays and mammalian assays supported by in  
27 vitro and non-mammalian assays

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- 1       • Consistent results in a diverse array of assays that evaluate different types of effects on  
2       genetic material (e.g., assays covering several rows in Table 3-12)

3  
4       If there are no studies for genotoxicity, enter “no data” into the spreadsheet. The determinant  
5       score when appropriate data are available is 5 for genotoxicity. Leave blank if there are no data.

6       **Table 3-14: Criteria for Genotoxicity Endpoint**

NIOSH Banding Criteria for <b>Genotoxicity</b>		
<b>Endpoint Band</b>		
<b>A</b>	<b>C</b>	<b>E</b>
Negative Results	Mixed results	Positive Results

7       **Endpoint Determinant Score – Genotoxicity**

8       If acceptable data point on genotoxicity is available, a score of 5 is assigned to the endpoint  
9       determinant score. The presence of multiple acceptable studies also warrants a score of 5. If  
10      there are no available data for genotoxicity, no band is assigned for genotoxicity and a  
11      determinant score of 0 is assigned. This score is assigned on the availability of the information,  
12      irrespective of the outcome of the test or observation (positive/negative).

13

1 **3.7. Banding Potentially Hazardous Chemicals on the Basis of Respiratory**  
 2 **Sensitization**

3 Sensitization can be differentiated into two subclasses: respiratory sensitization and skin  
 4 sensitization. A *respiratory sensitizer* is “a substance that will lead to hypersensitivity of the  
 5 airways following inhalation of the substance.” [UNECE 2013]. This chapter discusses  
 6 respiratory sensitization.

7 In Tier 2, respiratory sensitizers are allocated bands using qualitative data. If epidemiological or  
 8 clinical dose-response data are available for respiratory sensitization, the resulting  
 9 NOAELs/BMDLs are considered under the specific target organ toxicity endpoint.

10 **Data Sources – Respiratory Sensitization**

11 Sources for Tier 2 information for respiratory sensitization can be found in Table 3-15.

12 **Table 3-15: Data Sources for Respiratory Sensitization Endpoint**

<b>ENDPOINT</b>	<b>Rank</b>	<b>SOURCE OF INFORMATION</b>	<b>ACRONYM</b>
<b>Respiratory sensitization</b>	1	Organization for Economic Co-operation and Development	OECD
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
	2	Agency for Toxic Substances & Disease Registry	ATSDR
		U.S. EPA Integrated Risk Information System	IRIS
		Association of Occupational and Environmental Clinics	AOEC

13 **Classification Criteria – Respiratory Sensitization**

14 For a Tier 2 assessment, human or animal data are needed to assign a respiratory sensitization  
 15 band to a substance. These data are generally available from authoritative reviews conducted by  
 16 governmental, national, international, and professional agencies, a selection of which are listed in  
 17 Table 3-15.

18 Respiratory sensitization or respiratory allergy refers to an allergic reaction in the respiratory  
 19 tract (e.g., asthma) following exposure to the chemical. Respiratory sensitization does not refer  
 20 to irritation or damage to pulmonary tissue following chemical exposure. These outcomes would  
 21 be considered for banding under specific target organ toxicity after repeated or prolonged  
 22 exposure. Acute or single exposure respiratory irritation is not used in the OEB protocol.  
 23 According to the OSHA HCS, “sensitization includes two phases: the first phase is induction of  
 24 specialized immunological memory in an individual by exposure to an allergen. The second  
 25 phase is elicitation, i.e., production of a cell-mediated or antibody-mediated allergic response by  
 26 exposure of a sensitized individual to an allergen.” Evidence of respiratory sensitization is often

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1 based upon human evidence. Frequently it is seen as asthma, but other symptoms of allergic  
2 reactions such as runny nose and watery eyes (rhinitis/conjunctivitis) and inflammation in the  
3 lungs (e.g., alveolitis) are also considered.

4 Generally, to assess respiratory sensitization risk, regulatory agencies have adopted a qualitative  
5 approach as a first step. Because of lack of validated assay protocols that provide quantitative  
6 human or animal data on respiratory sensitization, GHS [UNECE 2013] has proposed no specific  
7 quantitative potency criteria for Category 1 respiratory sensitizers.

8 NIOSH recommends banding criteria for respiratory sensitization on the basis of qualitative  
9 criteria, as set forth in Table 3-16. Given the imprecise nature of the cut-points for banding this  
10 endpoint, some latitude is available for persons to use a qualitative approach, on the basis of the  
11 total evidence.

12

13 **Table 3-16: Criteria for Respiratory Sensitization Endpoint**

NIOSH Banding Criteria for <b>Respiratory Sensitization</b>		
<b>Endpoint Band</b>		
<b>A</b>	<b>C</b>	<b>E</b>
No evidence of respiratory sensitization	Mixed results	Positive evidence of respiratory sensitization

14 **Approach to Data Selection – Respiratory Sensitization**

15 Although no validated quantitative animal bioassays currently exist from which a reliable point  
16 of departure can be identified, inferential evidence on a chemical’s potential to induce this  
17 response can be drawn from conclusions provided in reviews from recommended databases (e.g.,  
18 ATSDR, IRIS, REACH assessments, OECD SIDS, etc.)

19 **Endpoint-Specific Band Selection – Respiratory Sensitization**

20 The following steps are followed to assign a band:

- 21 (1) Assign band E, if the classification system indicates the substance is a respiratory  
22 sensitizer.
- 23 (2) Assign band C, if results from these sources are mixed or the evidence is determined to  
24 be inconclusive.
- 25 (3) Assign band A if the classification system or evidence indicates the substance is not a  
26 respiratory sensitizer.

27

1 **3.8. Banding Potentially Hazardous Chemicals on the Basis of Skin Sensitization**

2 In addition to respiratory sensitization, the banding process evaluates a chemicals potential to  
 3 cause skin sensitization. A *skin sensitizer* is “a substance that will lead to an allergic response  
 4 following skin contact” [UNECE 2013].

5 In Tier 2, skin sensitizers are assigned to one of five endpoint bands, ranging from band E  
 6 (extreme sensitizers) to band A (non-sensitizers), on the basis of local lymph node assay (LLNA)  
 7 EC3 value ranges or other standard assays. EC3 is defined as the effective concentration  
 8 necessary to produce a stimulation index of 3 or more.

9 **Data Sources – Skin Sensitization**

10 Sources for Tier 2 information for skin sensitization can be found in Table 3-17.

11 **Table 3-17: Data Sources for Skin Sensitization Endpoint**

<b>ENDPOINT</b>	<b>Rank</b>	<b>SOURCE OF INFORMATION</b>	<b>ACRONYM</b>
<b>Skin sensitization</b>	1	NIOSH Skin Notation Profiles	SK Profiles
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
		Organization for Economic Co-operation and Development	OECD
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
	2	Hazardous Substance Data Bank	HSDB

12 **Classification Criteria – Skin sensitization**

13 Skin sensitization or skin allergy refers to an allergic reaction of the skin (e.g., allergic contact  
 14 dermatitis) following exposure to the chemical. Skin sensitization does not refer to irritation and  
 15 corrosion to skin following chemical exposure; these outcomes are a measure of Skin Corrosion  
 16 and Irritation that are addressed as a separate endpoint in this occupational exposure banding  
 17 process. According to the OSHA HCS, “sensitization includes two phases: the first phase is  
 18 induction of specialized immunological memory in an individual by exposure to an allergen. The  
 19 second phase is elicitation, i.e., production of a cell-mediated or antibody-mediated allergic  
 20 response by exposure of a sensitized individual to an allergen.” Evidence of skin sensitization in  
 21 humans is usually assessed by a diagnostic patch test. Evidence for skin sensitization in standard  
 22 animal assays includes the local lymph node assay, the guinea pig maximization test, and the  
 23 Buehler assay.

24 NIOSH has partially established its sensitization banding criteria on GHS. GHS has proposed  
 25 specific quantitative potency criteria for Category 1 (subcategories 1A and 1B) skin sensitizers.  
 26 These criteria are based on human evidence, EC3 values in the mouse LLNA, and the percentage  
 27 of positive animals in relation to the induction concentration tested in guinea pig maximization

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1 test and Buehler guinea pig test. GHS acknowledges that “human data are not generated in  
2 controlled experiments for the purpose of hazard classification but rather as part of risk  
3 assessment to confirm lack of effects seen in animal tests” [UNECE 2013]. Therefore, evidence  
4 from animal studies is often used and supplemented by observational data drawn from situations  
5 where humans have become exposed in either the workplace or environment.

6 In a Tier 2 assessment, data for assigning a band for skin sensitization are gathered and evaluated  
7 from authoritative reviews. Both qualitative and quantitative criteria are outlined in Table 3-18.  
8 In the case that both qualitative and quantitative data exist for this endpoint, each should be  
9 surveyed against the NIOSH skin sensitization criteria, and whichever data provide the most  
10 health protective band should be used. The NIOSH skin notation assignment can also be used to  
11 assign a band for skin sensitization as indicated in Table 3-18.

12 If LLNA EC3 values are available, the chemical is assigned one of five potency categories (A–E)  
13 on the basis of their associated threshold concentrations with respect to skin sensitization hazard.  
14 In the absence of LLNA EC3 values, NIOSH recommends using incidence of sensitization in  
15 relation to the induction concentration tested in GPMT and Buehler test, based on 2012  
16 European Chemical Agency recommendations.

17 **Table 3-18: Criteria for Skin Sensitization Endpoint**

NIOSH Banding Criteria for <b>Skin Sensitization</b>			
Test Type	Endpoint Band		
	A	C	E
EC3 (%) (based on LLNA)	Non-skin sensitizer	EC3 (%) $\geq 2.0 \leq 100$ (weak to moderate skin sensitizer)	EC3 (%) $\leq 2.0$ (strong to extreme skin sensitizer)
GPMT	No positive response or low incidence data	30% to 60% responding at $> 0.1\%$ intradermal induction concentration OR $\geq 30\%$ responding at $> 1\%$ intradermal induction concentration	$\geq 30\%$ responding at $\leq 0.1\%$ intradermal induction concentration OR $\geq 60\%$ responding at $> 0.1\%$ to $\leq 1\%$ intradermal induction concentration
Buehler	No positive response or low incidence data	$\geq 60\%$ responding at $> 0.2$ to $\leq 20\%$ topical induction dose OR $\geq 15\%$ responding at $> 20\%$ topical induction dose	$\geq 15\%$ responding at $\leq 0.2\%$ topical induction concentration OR $\geq 60\%$ responding at any topical induction concentration

18 **Approach to Data Selection – Skin Sensitization**

19 Band the chemical based on the LLNA EC3 value or the incidence data for skin sensitization.  
20 Select the most health-protective band as the final band. When quantitative skin sensitization  
21 data are available from more than one assay, select the band that is most health-protective.

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1 Qualitative data will determine band assignments only in the absence of quantitative data, as  
2 quantitative data take precedence.

### 3 **Endpoint-Specific Band Selection – Skin Sensitization**

4 Although human data are the most desirable source of evidence for this hazard class and the  
5 associated bands, skin sensitization band selection can use data from standard animal studies in  
6 mice (LLNA) and guinea pigs (Buehler test) from authoritative organizations.

7 The following steps are followed to assign a band:

8 (1) Consult authoritative reviews (Table 3-17) to identify reliable LLNA EC3 or sensitization  
9 incidence data reported in Buehler guinea pig test for a chemical. For banding purposes, these  
10 are compared to the technical criteria set forth in Table 3-18.

11 (2) Assign a band based on mouse LLNA EC3 value and/or Buehler test incidence data for  
12 sensitization.

13 (3) If multiple LLNA EC3 values and/or incidence data for sensitization from Buehler test are  
14 available, the most health-protective value or incidence data is used.

15 (4) If no quantitative EC3 value or incidence data are available, criteria for banding the skin  
16 sensitization endpoint are based on qualitative skin sensitization data gathered from the  
17 recommended sources according to Table 3-17.

### 18 **Endpoint Determinant Score – Respiratory and Skin Sensitization**

19 The availability of data to support conclusions provided in authoritative reviews can be based on  
20 observational information in humans or experimental data in animals on respiratory sensitization.  
21 If appropriate data for banding are available, this contributes an EDS of 10 in the overall  
22 assessment of whether sufficient information is available for banding a chemical in Tier 2. The  
23 availability of data on skin sensitization contributes an EDS of 5 in the overall assessment of  
24 whether sufficient information is available for banding a chemical in Tier 2. These scores are  
25 assigned on the availability of the information, regardless of the outcome of the test or  
26 observation (positive/negative).

27

### 3.9. Banding Potentially Hazardous Chemicals on the Basis of Acute Toxicity

Acute toxicity refers to those “adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.” [UNECE 2013]

When acute toxicity data are used for hazard banding, chemicals are assigned to one of five bands according to numerical values expressing the LD<sub>50</sub> (for oral or dermal exposure) or the median lethal concentration (LC<sub>50</sub>) (for inhalation exposure). The LD<sub>50</sub> and LC<sub>50</sub> represent the doses or concentrations that result in the death of 50% of the exposed group within an appropriate time, usually 14 days, after a single exposure.

#### Data Sources – Acute Toxicity

Sources for Tier 2 information for Acute Toxicity can be found in Table 3-19.

**Table 3-19: Data Sources for Acute Toxicity Endpoint**

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Acute Toxicity	1	National Library of Medicine ChemID Plus	ChemID Plus
		U.S. EPA Superfund Chemical Data Matrix	U.S. SCDM
		Pesticide Properties Database	PPDB
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
	2	Hazardous Substance Data Bank	HSDB
		Agency for Toxic Substances & Disease Registry	ATSDR

#### Classification Criteria for the Bands – Acute Toxicity

The banding scheme uses five categories (A to E) in which band E is the most precautionary. The numerical criteria (cut-points) for the LD<sub>50</sub>s and 4-hour LC<sub>50</sub>s are given in Table 3-20.

#### Approach to Data Selection – Acute Toxicity

Banding a chemical for acute toxicity in Tier 2 involves searching through NIOSH-recommended literature sources listed in Table 3-19 and recording all available LD<sub>50</sub> and LC<sub>50</sub> values for the chemical. A spreadsheet is provided for this purpose in Appendix B. The lowest (most health-protective) value by exposure route is used to determine the appropriate band according to the LD<sub>50</sub>/LC<sub>50</sub> technical criteria shown in Table 3-20. This determination is then entered into the Tier 2 checklist in the appropriate row and column.

A determinant score of 5 is entered if any acceptable acute lethality data are available for the chemical in question. If more than one type of acute lethality data are available for a chemical under investigation, for example, an oral LD<sub>50</sub> *and* an inhalation LC<sub>50</sub>, the acute toxicity determinant score remains at 5.

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1 **Table 3-20: Criteria for the Acute Toxicity Endpoint**

NIOSH banding criteria for <b>Acute Toxicity</b>					
Exposure/Dosing Route	Endpoint Band				
	A	B	C	D	E
<b>Oral toxicity (LD<sub>50</sub>)</b>	>2,000 mg/kg- bodyweight	>300 to ≤ 2,000 mg/kg- bodyweight	>50 to ≤ 300 mg/kg- bodyweight	>5 to ≤ 50 mg/kg- bodyweight	≤ 5 mg/kg- bodyweight
<b>Dermal toxicity (LD<sub>50</sub>)</b>	> 2,000 mg/kg- bodyweight	>1,000 to ≤ 2,000 mg/kg- bodyweight	>200 to ≤ 1,000 mg/kg- bodyweight	>50 to ≤ 200 mg/kg- bodyweight	≤ 50 mg/kg- bodyweight
<b>Inhalation gases (LC<sub>50</sub>)</b>	> 20,000 ppmV/4h	>2,500 to ≤ 20,000 ppmV/4h	>500 to ≤ 2,500 ppmV/4h	>100 to ≤ 500 ppmV/4h	≤ 100 ppmV/4h
<b>Inhalation vapors (LC<sub>50</sub>)</b>	> 20.0 mg/liter/4h	>10.0 to ≤ 20.0 mg/liter/4h	>2.0 to ≤ 10.0 mg/liter/4h	>0.5 to ≤ 2.0 mg/liter/4h	≤ 0.5 mg/liter/4h
<b>Inhalation dusts and mists (LC<sub>50</sub>)</b>	> 5.0 mg/liter/4h	>1.0 to ≤ 5.0 mg/liter/4h	>0.5 to ≤ 1.0 mg/liter/4h	>0.05 to ≤ 0.5 mg/liter/4h	≤ 0.05 mg/liter/4h

2

3 **Rules for Accepting or Rejecting Lethality Data for Band Selection – Acute Toxicity**

4 Acute toxicity data may be available from a variety of different types of studies, some of which

5 may be more reliable and relevant to banding than others. Not all acute toxicity values are

6 appropriate for banding. Use the following rules to accept or reject data points for band selection:

- 7
- 8
- 9
- 10
- 11
- 12
- 13
- Only values from studies using routinely employed experimental animals such as rats, mice, rabbits, guinea pigs, etc. should be employed for banding. Values from species that are less likely to be adequate models for toxicity in humans (such as chicken, frog, etc.) should not be used for banding.
  - Studies where the administration of the chemical dose was other than oral, dermal, or inhalation (e.g., subcutaneous, intraperitoneal, intravascular) should be rejected and not used for banding.

14 **Other conditions requiring rejection for banding purposes include:**

- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- Studies where the experimental animal is not stated
  - Studies where the experimental animal is described as “mammal(s)”
  - Lethality data that do not reflect the median lethal dose, such as LD<sub>10</sub>, or LD<sub>LO</sub>, etc.
  - Values preceded by a greater than (>) symbol, where the numerical value falls within the criteria for bands B–E
  - Values from experiments in which more than a single dose was administered
  - Values presented as a range of concentrations, where any of the numerical values in the range fall within the criteria for bands B–E, except when the range refers to separate values for male and female (e.g., LD<sub>50</sub> of 2 mg/kg for males and 10 mg/kg for females)

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1 reported as a range of 2–10 mg/kg). In that case, the low end of the range is used for  
2 banding.

3 For LC<sub>50</sub> values, the following additional rules apply:

4 Studies where the exposure duration is unknown should be rejected because the concentrations  
5 cannot be scaled to the standard 4-hour exposure regimen. If the exposure duration is known but  
6 was other than 4 hours, the LC<sub>50</sub> should be converted to a 4-hour equivalent. While Haber’s rule  
7 (simple proportionality) is sometimes used for these types of conversions, NIOSH recommends  
8 using the ten Berge equation:

$$9 \quad \text{Adjusted LC}_{50} (4 \text{ hours}) = \text{LC}_{50}(t) \times ((t/4)^{(1/n)})$$

10 Where: LC<sub>50</sub> (t) = LC<sub>50</sub> determined over t hours from the study being used; and t is the number  
11 of hours of exposure in the study being used to estimate the 4-hour equivalent value

12 n = the ten Berge constant [ten Berge et al. 1986]. A default value of 1 is used for “n” when  
13 extrapolating to longer durations and a default value of 3 is used for “n” when extrapolating to  
14 shorter durations.

15 Table 3-21 gives (1) a list of adjustment factors, (2) the resulting 4-hour LC<sub>50</sub> calculated for an  
16 experimentally derived value of 100 mg/m<sup>3</sup> for the different exposure periods, and (3) the  
17 comparable 4-hour LC<sub>50</sub> values determined through the simple application of simple  
18 proportionality (Haber’s rule). This adjustment table is not specific to the physical form of the  
19 chemical, and can be applied for particles and vapors/gases.

20 **Table 3-21: Duration Adjustment Factors for Acute Toxicity**

Exposure duration (hours)	ten Berge constant	Adjustment factor	Derived 4-hour LC <sub>50</sub>	Comparable 4-hour LC <sub>50</sub> s by Haber’s rule
1	1	0.25	25	25
2	1	0.5	50	50
3	1	0.75	75	70
4	1	1	100	100
5	3	1.08	108	125
6	3	1.14	114	150
7	3	1.2	120	175
8	3	1.26	126	200
9	3	1.31	131	225
10	3	1.36	136	250

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1 As shown in Table 3-21, for exposures longer than 4 hours, the derived 4-hour LC<sub>50</sub> values are  
2 lower, and thus more health-protective than those calculated using Haber's rule. It is conceivable  
3 that this difference may affect band selection for some chemicals.

4

5 After making appropriate conversions, the user should enter the values in the appropriate units  
6 (ppm/4 hours or milligrams per liter of air/4 hours) according to whether the agent is a gas,  
7 vapor, or dust/mist. For banding purposes, the appropriate cut-points for LC<sub>50</sub> values associated  
8 with agents in different physical forms are given in Table 3-20. An explanatory note with  
9 applicable definitions is given in the Addendum.

### 10 **Endpoint-Specific Band Selection – Acute Toxicity**

11 When all the acceptable LD<sub>50</sub> and LC<sub>50</sub> data have been assembled by data source for each route  
12 (oral, dermal, inhalation), the lowest value will be compared to the technical criteria for band  
13 selection. The spreadsheet enters the selected band in the column headed Endpoint-specific band  
14 selection (right-hand side) based on the most stringent band among all the routes with acceptable  
15 LD<sub>50</sub> or LC<sub>50</sub> values.

### 16 **Endpoint Determinant Score – Acute Toxicity**

17 If at least one acceptable data point is available, a score of 5 is assigned to the endpoint  
18 determinant score. The presence of multiple acceptable data points also warrants a score of 5. If  
19 there are no available values for a particular acute toxicity/lethality endpoint, no band is assigned  
20 for acute toxicity and a determinant score of 0 is assigned.

21

22

23

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28

1 **3.10. Banding Potentially Hazardous Chemicals on the Basis of Skin Corrosion and**  
 2 **Irritation**

3 Skin corrosion is “the production of irreversible damage to the skin; namely, visible necrosis  
 4 through the epidermis and into the dermis, following the application of a test substance for up to  
 5 4 hours.” These corrosive reactions are typified by ulcer, bleeding, bloody scabs, and, at the end  
 6 of a 14-day observation period, by discoloration due to blanching of the skin, complete areas of  
 7 alopecia, and scars. *Skin irritation* is defined as “the production of reversible damage to the skin  
 8 following the application of a test substance for up to 4 hours.” [UNECE 2013]. Direct effects on  
 9 the skin can be defined as nonimmune mediated (non-allergic) adverse health effects resulting in  
 10 damage or destruction of the skin localized at or near the point of contact [NIOSH 2009b].  
 11 Common manifestations of direct effects in addition to irritation/corrosion include: (1)  
 12 permanent pigmentation changes (i.e., bleaching or staining of the skin), (2) nonimmune  
 13 phototoxic reaction and (3) defatting that leads to great susceptibility of the skin to toxic  
 14 exposures. Many direct skin effects can affect the skin barrier integrity resulting in an increased  
 15 potential of chemical penetration and subsequent risk of systemic toxicity [NIOSH 2009b].  
 16 Direct effects on the skin beyond irritation/corrosion are not defined or included in the GHS  
 17 decision process. Despite their absence from GHS, these effects may have substantial adverse  
 18 effects on the lives and health of workers. In-depth descriptions of these health endpoints, in  
 19 addition to supplemental information useful for hazard characterization purposes of such direct  
 20 skin effects beyond irritation and corrosion, are available in the NIOSH Current Intelligence  
 21 Bulletin Number 61 [NIOSH 2009b].

22 **Data Sources – Skin Corrosion/Irritation**

23 Sources for Tier 2 information for skin corrosion/irritation can be found in Table 3-22.

24 **Table 3-22: Data Sources for Skin Corrosion/Irritation Endpoint**

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Skin Irritation	1	NIOSH Skin Notation Profiles	SK Profiles
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
		Organization for Economic Co-operation and Development	OECD
	2	Agency for Toxic Substances & Disease Registry	ATSDR
		U.S. EPA Integrated Risk Information System	IRIS

25

26 **Classification Criteria – Skin Corrosion/Irritation**

27 For the Tier 2 assessment, information for assigning a skin corrosion/irritation band to a  
 28 substance is generally available from authoritative reviews conducted by governmental, national,

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1 international, and professional agencies throughout the world as listed in Table 3-22. GHS  
2 [UNECE 2013] has proposed criteria for Categories 1 and 2, but not Category 3, skin  
3 corrosion/irritation substances. NIOSH has not recommended band assignments on the basis of  
4 potency information (e.g., dose-response data, Draize scores) for skin corrosion/irritation  
5 substances under Tier 2 assessments. Where dose-response data are available for irritation or  
6 other direct effects, such data may be used as part of the STOT endpoint. The recommended  
7 NIOSH criteria shown in Table 3-23 assigns bands for skin corrosion/irritation based on  
8 classification systems from authoritative organizations.

9 **Table 3-23: Criteria for Skin Corrosion/Irritation Endpoint**

NIOSH Banding Criteria for <b>Skin Irritation/Skin Corrosion</b>			
<b>Endpoint Band</b>			
<b>A</b>	<b>B</b>	<b>C</b>	<b>E</b>
Non-irritating	Mild to moderate irritation	Moderate to severe irritation; reversible direct effects OR If results are mixed or indicate irritant potential with severity unspecified	Skin corrosion; irreversible effects  pH value of $\leq 2.0$ or $> 11.5$

10

### 11 **Approach to Data Selection – Skin Corrosion/Irritation**

12 The following provide information on the potential of a substance to be assigned a band based on  
13 the Skin Corrosion/Irritation endpoint:

- 14 • Classification system from an authoritative organization (e.g., NIOSH skin notation  
15 strategy)[NIOSH 2009b]
- 16 • Conclusions provided by authoritative reviews (e.g., ATSDR, European Chemicals Agency,  
17 IRIS, Organisation for Economic Co-operation and Development Screening Information  
18 Data Set, REACH assessments)

19

20 When multiple classifications or conclusions by various authoritative reviews are present, the  
21 most health-protective band corresponding to those conclusions is selected. The assessment is  
22 based on the substance in pure form, unless banding is being developed for a specific product  
23 that includes diluted or non-concentrated material. For example, a strong acid such as  
24 hydrochloric acid banded using this process would be classified as band E for the Skin  
25 corrosion/irritation endpoint, even though non-concentrated dilutions can be non-irritating.

### 26 **Endpoint-Specific Band Selection – Skin Corrosion/Irritation**

27 NIOSH recommends the following potency criteria for assigning bands for the Skin  
28 corrosion/irritation endpoint under Tier 2 assessment Table 3-23, the findings based on  
29 classification systems provided by authoritative organizations or conclusions provided in  
30 authoritative reviews (Table 3-22).

71

*This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by the National Institute for Occupational Safety and Health. It does not represent and should not be construed to represent any agency determination or policy.*

## DRAFT

1 For skin irritation or corrosion, the following guidance is provided:

- 2 • Assign band E if the substance is characterized by *skin corrosion*.
- 3 • Assign band C if the substance is characterized as a *moderate skin irritant*, or if results  
4 are mixed or indicate the potential for skin irritation, but do not specify severity.
- 5 • Assign band B if the substance is characterized as *mild or weak irritant*.
- 6 • Assign band A if the substance is not a *skin irritant*.
- 7 • Other indications that a chemical causes irritation include qualitative descriptions that  
8 suggest that the chemical is associated with erythema, peeling skin, dry or cracked skin,  
9 reddening, swelling, and/or itching of the skin. These descriptors can be used to band  
10 skin irritants based on the severity of the reaction. Reversible, mild effects that occur at  
11 high concentrations should be placed into bands B and C, while serious, irreversible  
12 effects that occur at low concentrations are banded in bands D and E.

13 For direct effects on the skin other than skin irritation/corrosion, the following guidance is  
14 provided:

- 15 • Assign band C if the substance is identified to cause a reversible direct effect on the skin  
16 other than irritation/corrosion, or if results indicate the potential for a direct effect of the  
17 skin associated with a nonimmune mediated mechanism, but does not specific severity.

### 18 **Endpoint Determinant Score – Skin Corrosion and Irritation**

19 The availability of adequate data to support conclusions provided in authoritative reviews can be  
20 based on (1) observational information in humans who are topically exposed to a chemical in the  
21 workplace or in an emergency situation or (2) experimental data on skin corrosion and irritation  
22 or other direct effects on the skin that are associated with a nonimmune mediated mechanism in  
23 experimental animals. If data that can be used for banding have been provided by the  
24 authoritative reviews, this contributes an EDS of 5 in the overall assessment of whether  
25 sufficient information is available for banding a chemical in Tier 2. This EDS is assigned on the  
26 availability of the information, irrespective of the outcome of the test or observation  
27 (positive/negative).

1 **3.11. Banding Potentially Hazardous Chemicals on the Basis of Eye**  
 2 **Damage/Irritation**

3 *Serious eye damage* is “the production of tissue damage in the eye, or serious physical decay of  
 4 vision, following application of a test substance to the anterior surface of the eye, which is not  
 5 fully reversible within 21 days of application.” *Eye irritation* is defined as “the production of  
 6 changes in the eye following the application of test substance to the anterior surface of the eye,  
 7 which are fully reversible within 21 days of application” [UNECE 2013].

8 **Data Sources – Eye Damage/Irritation**

9 Sources for Tier 2 information for Eye Damage/Irritation can be found in Table 3-24.

10 **Table 3-24: Data Sources for Eye Damage/Eye Irritation Endpoint**

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Eye Irritation	1	Organization for Economic Cooperation and Development	OECD
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
	2	Agency for Toxic Substances & Disease Registry	ATSDR
		U.S. EPA Integrated Risk Information System	IRIS

11 **Classification Criteria – Eye Damage/Irritation**

12 For a Tier 2 assessment, data for assigning a band to a substance based on its capacity to cause  
 13 serious eye damage or irritation are gathered and evaluated from authoritative reviews conducted  
 14 by governmental, national, international, and professional agencies with interests in the human  
 15 health impacts of hazardous chemicals (Table 3-24). However, for a Tier 2 assessment, NIOSH  
 16 has not recommended band assignments based on potency information (e.g., dose-response data,  
 17 Draize scores, etc.) for the eye damage/eye irritation endpoint. Instead, NIOSH recommends  
 18 assigning bands on the basis of qualitative data provided by authoritative reviews as shown in  
 19 Table 3-25.

20 **Table 3-25: Criteria for Eye Damage/Eye Irritation Endpoint**

NIOSH Banding Criteria for <b>Serious Eye Damage/Eye Irritation</b>			
Endpoint Band			
A	B	C	E
Non-irritating	Mild to moderate irritation	Severe irritation; moderate to severe irritation OR Irritant with unspecified severity, no conclusion, or mixed results	Irreversible eye damage

## DRAFT

### 1 **Data Quality Assessment Parameters – Eye Damage/Irritation**

2 The following provides information on the potential of a substance to be assigned a band based  
3 on the Eye Damage/Eye Irritation endpoint:

- 4 • Conclusions provided in authoritative reviews (e.g., ATSDR, IRIS, OECD SIDS, ECHA  
5 dossiers)
- 6 • When multiple classifications by various authoritative reviews exist, the most health  
7 protective band corresponding to the classifications is selected (Table 3-25)

### 8 **Endpoint Specific Band Selection –Eye Damage/Eye Irritation**

- 9 (1) Assign band E if the substance is characterized as causing *irreversible eye damage*.
- 10 (2) Assign band C if the substance is characterized as a *severe eye irritant, moderate to*  
11 *severe eye irritant*, or if results are mixed.
- 12 (3) Assign band B if the substance is characterized as *mild to moderate irritation*.
- 13 (4) Assign band A if the substance is not an eye irritant.

### 14 **Endpoint Determinant Score – Eye Damage/Eye Irritation**

15 The availability of adequate data to support conclusions provided in authoritative reviews can be  
16 based on (1) observational information in humans who are splashed in the eye with a chemical or  
17 exposed to its vapor in the workplace or in an emergency situation and/or (2) experimental data  
18 on eye corrosion and irritation in experimental animals. If a conclusion has been provided by the  
19 authoritative reviews, this contributes a determinant score of 5 in the overall assessment of  
20 whether sufficient information is available for banding a chemical in Tier 2. This score is  
21 assigned on the availability of the information, irrespective of the outcome of the test or  
22 observation (positive/negative).

### 3.12. Issues of Certainty Bounding Band Selection

In deriving a TDS as an index of data sufficiency for banding, the measure addresses the range of toxicological endpoints that are identified for a particular compound but not the *number* of studies within each toxicological category. Given the higher degree of certainty associated with multiple studies of each endpoint, it is likely that varying degrees of certainty on band selection will be determined for chemicals where the TDS is similar. This is to be expected, and users may wish to take this factor into consideration when banding chemicals. NIOSH has not developed specific guidance on this point.

### 3.13. Applicability and Suggested Rules for Using Human Data for Hazard Banding

This section addresses the use of qualitative and quantitative human data in band selection at the Tier 2 level. For endpoints where a dose-response analysis and the identification of a toxicity threshold is required for band selection (reproductive and/or developmental toxicity, specific target organ toxicity through repeated exposure, and carcinogenicity), the desirability of using quantitative human data centers on the possibility of reducing uncertainty in extrapolating dosimetric data obtained in experimental animals to health deficits that might occur in exposed humans. However, toxicological data in environmentally or occupationally exposed human cohorts are often beset by imprecision in the exposure term, uncertain duration, and the likelihood of concurrent exposure to other chemicals. In practice, therefore, comparatively few well-documented human exposure data sets are available for dose-response analysis and band selection.

For endpoints where a categorical outcome can be evaluated on a qualitative or semi-quantitative basis, information on such endpoints as skin and eye irritation and skin and respiratory sensitization may be available from exposed groups or through testing in volunteers. Simple statements covering the presence of an effect or the severity of the outcome (no effect, mild, severe) may contribute to our understanding of the possible impact of the chemical on these endpoints, and thus apply to their banding, in accordance with applicable technical criteria. The following paragraphs give some simple rules for using quantitative and qualitative human exposure information for banding at the Tier 2 level.

#### Quantitative Information

Human data may be applicable for hazard banding in Tier 2 if the following criteria apply:

- (1) The data have been obtained from Rank 1 sources.
- (2) Agencies have used them to develop toxicity benchmarks, such as an RfC (U.S. EPA) or MRL (ATSDR).
- (3) A dose-related response is evident from the principal study, with a clearly defined NOAEL.

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1 NOTE: *The use of human exposure data from Rank 2 sources is not recommended for banding*  
2 *because, in many if not all cases, the dosimetry is likely to be less reliable, and, by analogy to the*  
3 *rules for determining an animal-specific NOAEL, the dose-dependent human health deficits and*  
4 *related points-of-departure may be less clear-cut.*

### 5 Example where human exposure data are applicable

- 6 • The U.S. EPA's RfC for a 2,4- and 2,6-toluene diisocyanate mixture is based on a  
7 NOAEL of 0.006 mg/m<sup>3</sup> (0.0009 ppm) that was observed in a prospective occupational  
8 study with a decline in lung function as the primary effect [Diem et al. 1982]. A LOAEL  
9 of 0.014 mg/m<sup>3</sup> (0.0019 ppm) was given in the summary. **Band E** would apply to these  
10 findings.

### 11 An example where animal data better define the primary effect, though supported by human 12 exposure data

- 13 • The primary effect of chronic exposure to n-hexane is peripheral neuropathy. This effect  
14 has been described in a number of reports on health effects of shoe and leather-goods  
15 workers. However, because these reports contain imprecise information on exposure  
16 levels, the U.S. EPA's IRIS database developed an RfC for this compound on the basis of  
17 nervous system deficits in Wistar rats, the BMCL of 430 mg/m<sup>3</sup> (122 ppm) placing the  
18 chemical in **band D**. Surveying the accounts of epidemiological studies and reports in the  
19 IRIS toxicological review of n-hexane suggests a point-of-departure for the critical effect  
20 in the vicinity of 50 ppm, also applicable to **band D**. However, the latter estimate, while  
21 useful as a check, would itself be inadequate as the primary source for banding because it  
22 was not used to develop the RfC, and precise dose-response information is generally  
23 lacking.

### 24 **Qualitative Information**

25 Information on categorical outcomes such as skin and eye irritation and skin and respiratory  
26 sensitization may be obtained from human studies on the basis of simple summary statements to  
27 be found in secondary sources such as HSDB, EHC documents, and from other secondary  
28 documents as may apply to the chemical under evaluation.

### 29 Example

- 30 • An illustration of the process may be obtained from consideration of the HSDB record for  
31 styrene. A suggested procedure would be to open the record for the chemical and (1)  
32 click on *Human Health Effects*; (2) track down through the record to the subheading *Skin,*  
33 *Eye, and Respiratory Irritations*; (3) document any relevant findings from the short  
34 paragraphs given in this section. For styrene, the chemical is said to be *irritating to skin,*  
35 *and that exposure to concentration of styrene above 200 ppm causes irritation of the eyes*  
36 *and respiratory tract.* **Band B** would be a reasonable selection for both outcomes, on the  
37 basis of these statements. However, a more precautionary band selection might be

1 warranted if skin and eye tests in animals give a more severe outcome such as skin  
2 corrosion or other irreversible effects.

### 3 **3.14. OEB – Considerations for Application of the Range of Concentrations**

4 The occupational exposure banding process uses a set of endpoint-specific criteria to identify the  
5 hazard-based band most representative of the health effects profile for the chemical being  
6 evaluated. Each band corresponds to a range of airborne concentrations to assist with risk  
7 management decisions.

8 The OEB range that is the product of the banding procedure contrasts with a traditional OEL,  
9 which is typically represented as a single value for risk management purposes. Despite the  
10 difference in the OEB and OEL derivation process, the interpretation and use of the band and  
11 associated concentration range is not very different from traditional occupational hygiene  
12 practice for OELs. The practical similarity in OEBs and OELs stems from the fact that OELs are  
13 not precise estimates of a cut-point between safe and dangerous. Most OELs are derived by  
14 weighing the relevant data in a process that includes selection of a measure of toxic potency (the  
15 point of departure) and application of uncertainty factors (which often are order of magnitude  
16 estimates). Like most OELs, an OEB can be used as a TWA with a specific duration of time,  
17 such as 8 hrs. An OEB can also be used for shorter durations, such as a 15-min STEL when  
18 useful. The range of uncertainty in an OEL depends on the level of confidence in the underlying  
19 data and the extrapolation involved. Overall, the OEB identified in using the procedure in this  
20 NIOSH guidance is intended to provide a credible range for risk management. Consequently, the  
21 NIOSH process requires a risk management structure that can accommodate the use of a range of  
22 guide values.

23 Many organizations apply the concept of hazard-based banding strategies, such as the NIOSH  
24 occupational exposure banding process, as a supportive component of a risk management  
25 strategy. Occupational exposure banding and related categorical hazard assessment processes are  
26 a key component of existing control banding techniques. The value of such a strategy is that it  
27 does not attempt to force inappropriate precision from the hazard analysis. A categorical view of  
28 the bands also aligns with the practical consideration that exposure control strategies are also  
29 categorical in nature. In practice, combinations of controls available for a given exposure  
30 scenario are not infinite. The use of the bands as control ranges is consistent with common  
31 applications of the control-banding procedure. Based on such an approach, an organization  
32 implementing the occupational exposure banding process might have a default suite of control  
33 requirements for each band. Thus, band A chemicals might require only standard workplace  
34 precautions, while a band E chemical might require use or handling only with full containment  
35 methods. Each control regime would have been vetted for ability to control to the lowest  
36 concentration in the band. In this case the lower end of the band is often used as the default  
37 exposure control. The use of the lower end of the band is the most health protective strategy if

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1 additional chemical-specific assessments are not being made to refine the OEB or the resulting  
2 default control strategies.

3 As an alternative to the use of a categorical approach, the OEB allows for further customization  
4 of risk management procedures by selecting a guide value range within the OEB. Some  
5 stakeholders may select a guide value range of 10% of the OEB range, whereas others use a  
6 guide value range including the median, or 75% of the OEB range. The decision of a guide value  
7 range should be based upon the individual scenario involved. Selection of any point estimate  
8 within the range would typically reflect a deeper level of evaluation of the data that provides  
9 more specificity than the Tier 2 process does, as written.

### 10 **3.15. Consideration of Special Categories of Aerosols**

11 The occupational exposure banding process for particles depends on toxicity assumptions that  
12 are generally based on information on aerosols in the range of 0.1 to 100 micrometers  
13 aerodynamic diameter (microscale particles). As for any chemical, the toxicity profile for  
14 microscale particles is a function of the dose received at the affected target site (e.g., different  
15 regions of the respiratory tract or other systemic targets following uptake into the blood). For  
16 airborne microscale and nanoscale (between 1 and 100 nanometers) particles, the amount (e.g.,  
17 total mass or surface area of the aerosol) that reaches and deposits in the target site in the  
18 respiratory tract has been associated with the extent and severity of effects in animals and  
19 humans [Green et al. 2007; Kuempel et al. 2009; Kuempel et al. 2014]. A dose-response  
20 relationship is observed when the incidence or severity of an effect becomes more probable or  
21 pronounced with increasing target tissue dose.

22 Some particles have unique physical characteristics that support modifications to the general  
23 occupational exposure banding process. This modification is needed to address the observation  
24 that the total mass dose delivered does not always describe well the dose-response behavior for a  
25 single chemical across all particulate sizes and forms. One well documented example is the  
26 respiratory tract toxicity of titanium dioxide (TiO<sub>2</sub>), which is associated with the total particle  
27 surface area dose retained in the lungs in rodent studies [NIOSH 2011]. As a result, the NIOSH  
28 REL for ultrafine (nanoscale) TiO<sub>2</sub> (0.3 mg/m<sup>3</sup>) is lower than the REL for fine (microscale) TiO<sub>2</sub>  
29 (2.4 mg/m<sup>3</sup>), by the same factor as the relative particle surface area of fine and ultrafine TiO<sub>2</sub>  
30 evaluated in the rodent studies [NIOSH 2011]. Other physical and/or chemical properties can  
31 also influence the degree of toxicity observed for inhaled particles (e.g., size, shape, surface  
32 reactivity, solubility). Examples of particle categories include liquid aerosols, fibers, and  
33 nanoparticles (defined as particles having at least one dimension of the primary particles <100  
34 nanometers [BSI 2007; ISO 2007, 2008; NIOSH 2009a; ISO 2014]). Recommendations for the  
35 application of the occupational exposure banding process for particles in these categories are  
36 described in this section.

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1 **Liquid aerosols.** Particulates in the liquid phase can be evaluated using the general occupational  
2 exposure banding process regardless of aerodynamic diameter. This reflects that the toxicity of  
3 liquid aerosols is typically driven by the interaction of molecules that reach cellular targets after  
4 the material has dissolved or thoroughly dispersed in biological fluids. Such molecular  
5 interactions are not expected to vary greatly among exposures to different particle size  
6 distributions of liquid materials (assuming equivalent molecular concentrations among liquid  
7 particle sizes). However, differences in the nature and severity of effects could still be observed  
8 to the extent that differences in particle sizes result in differences in deposited doses in the  
9 respiratory tract regions [Hinds 1982].

10 **Fibers.** Fibers have unique aerodynamic features that are dependent on their geometry (e.g.,  
11 length-to-width aspect ratio and cross-sectional diameter) and influence their deposition in the  
12 respiratory tract. In addition, the physical shape and size of fibers can directly influence  
13 toxicological properties and the nature of their interactions with target cells. These complexities  
14 require approaching fibers with a Tier 3 assessment, and the OEB criteria are not recommended  
15 [Hinds 1982].

16 **Nanoscale solid-phase particles.** For the purpose of this document nanoscale particles are  
17 defined as those particles with primary particle diameters less than 100 nanometers [NIOSH  
18 2009a]. Significant evidence indicates that for some poorly soluble particles, increases in toxic  
19 potency occur for a chemical when comparing the same mass dose of microscale and nanoscale  
20 materials (see review in NIOSH [2011]). However, the total particle surface area dose retained in  
21 the lungs in rodents was a good predictor of adverse lung effects [NIOSH 2011]. This finding  
22 has led to the conclusion that dose in terms of “total mass deposited” does not always adequately  
23 predict dose-response behavior or toxic potency across particle sizes. This difference might  
24 reflect increases in the available surface area for biochemical reactivity, increased bioavailability  
25 at the cellular level, or other factors. In addition, the deposition efficiency of nano-diameter  
26 particles in the respiratory tract is greater than that of micro-diameter particles, and a higher  
27 proportion of the airborne nano-diameter particles is capable of depositing in the pulmonary  
28 (gas-exchange) region of the lungs [Maynard and Kuempel 2005; Oberdörster et al. 2005].

29 These empirical data and mechanistic hypotheses have been used to support application of the  
30 hazard banding procedures within control banding schemes for engineered nanoparticles (e.g., as  
31 applied in [ANSES 2010; ISO 2014]). On the basis of similar criteria, NIOSH recommends that  
32 the occupational exposure banding process — when applied to nanoparticles — are modified  
33 according to the following guidelines:

- 34
- **Poorly-soluble nanoscale particles:**

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1 If the toxicity data include NOAELs that were developed specifically for the nanoscale  
2 form of the chemical, the NIOSH occupational exposure banding process can be used  
3 directly with no modifications.

4 If data are only available for the microscale form of the chemical the band assignment  
5 should be shifted to the next most potent band on the assumption that poorly soluble  
6 nanoscale agents will likely be an order of magnitude more toxic than their microscale  
7 equivalents.

8 This assumption is supported by evidence of an approximately 10-fold higher potency for  
9 some nano-diameter poorly-soluble particles compared to the same mass dose of micro-  
10 diameter particles (reflecting an approximately 10-fold difference in specific surface area,  
11 e.g., 5 vs. 50 m<sup>2</sup>/g) [NIOSH 2011].

12 • ***Soluble nanoscale particles:***

13 Data support a role of increased total particle surface in the increased toxicity associated  
14 with poorly-soluble nanoscale particles as discussed above. Thus, because the retained  
15 surface area is lower over time for soluble particles (due to dissolution), increased  
16 solubility would decrease the potency of particles *if* the adverse effects are due to the  
17 retained particle surface dose. On the other hand, higher solubility could result in  
18 increased potency (compared to poorly soluble particles) if the toxic effects are due to  
19 released ions. Ions can react with cells at either the site of entry, such as lungs, or in other  
20 organs, potentially causing tissue damage and decreased organ function at certain doses.  
21 Particle size may play less of a role in the toxicity of higher-solubility particles assuming  
22 similar molecular concentrations and ion release rates. Thus, as particle solubility  
23 increases, there may be less need for the OEB to account for enhanced toxicity due to the  
24 nanoparticle-specific characteristics. In the ANSES [2010] and International Standards  
25 Organization (ISO) [2014] control banding schemes, soluble particles (defined as  
26 solubility in water > 0.1 g/l) are addressed with regard to the toxicity of the solute,  
27 without consideration of nanoparticle-specific toxicity.

28 However, acceptance of these general conclusions requires caution because of limited  
29 data on which to evaluate their effectiveness. For example, data and methods are not yet  
30 available to predict adverse effects solely on the basis of specific physical-chemical  
31 properties, such as solubility. Moreover, moderately soluble particles may elicit effects  
32 related to both their particulate and solute components. Despite these knowledge gaps on  
33 the role of nanoscale characteristics on the potential toxicity of inhaled particles and  
34 fibers, some aspects of the enhanced toxicity observed with inhaled nanoscale particles  
35 may relate to higher respiratory tract deposition and bioavailability (which would also  
36 occur regardless of particle solubility). Given these uncertainties, it is recommended that  
37 in the absence of data to the contrary, all nanoscale particles should be treated in the same  
38 manner without regard to solubility. Accordingly, NIOSH recommends shifting the  
39 banding assignment to the next most potent band if data are only available for the  
40 microscale form of the agent.

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- 1 • *Nanoscale fibers (or tubes)*: Since the toxicity of nanoscale fibers and nanoscale tubes  
2 may differ significantly from other forms of the compound, the occupational exposure  
3 banding process described in this document may not fully and accurately capture the  
4 toxicity of these chemicals. Therefore, tier 1 and tier 2 should not be used. Instead, a Tier  
5 3 assessment is required as described for other fibers.

6 These general recommendations are considered precautionary in nature. Limitations in the  
7 available scientific information include uncertainty in the mechanisms of potential potency  
8 differences in toxicity of nanoscale vs. microscale particles of various chemical composition,  
9 surface properties, shape, degree of agglomeration, etc. The number of chemicals with adequate  
10 data for such size-based toxicity comparisons is small, which prevents drawing firm conclusions  
11 at this time about relative potencies among various particle types and sizes. NIOSH is currently  
12 evaluating the state of the science for deriving OELs or OEBs for nanomaterials [NIOSH 2014],  
13 and is also examining the process and data for developing hazard categories for nanomaterials  
14 based on biological mode of action and physical-chemical properties.

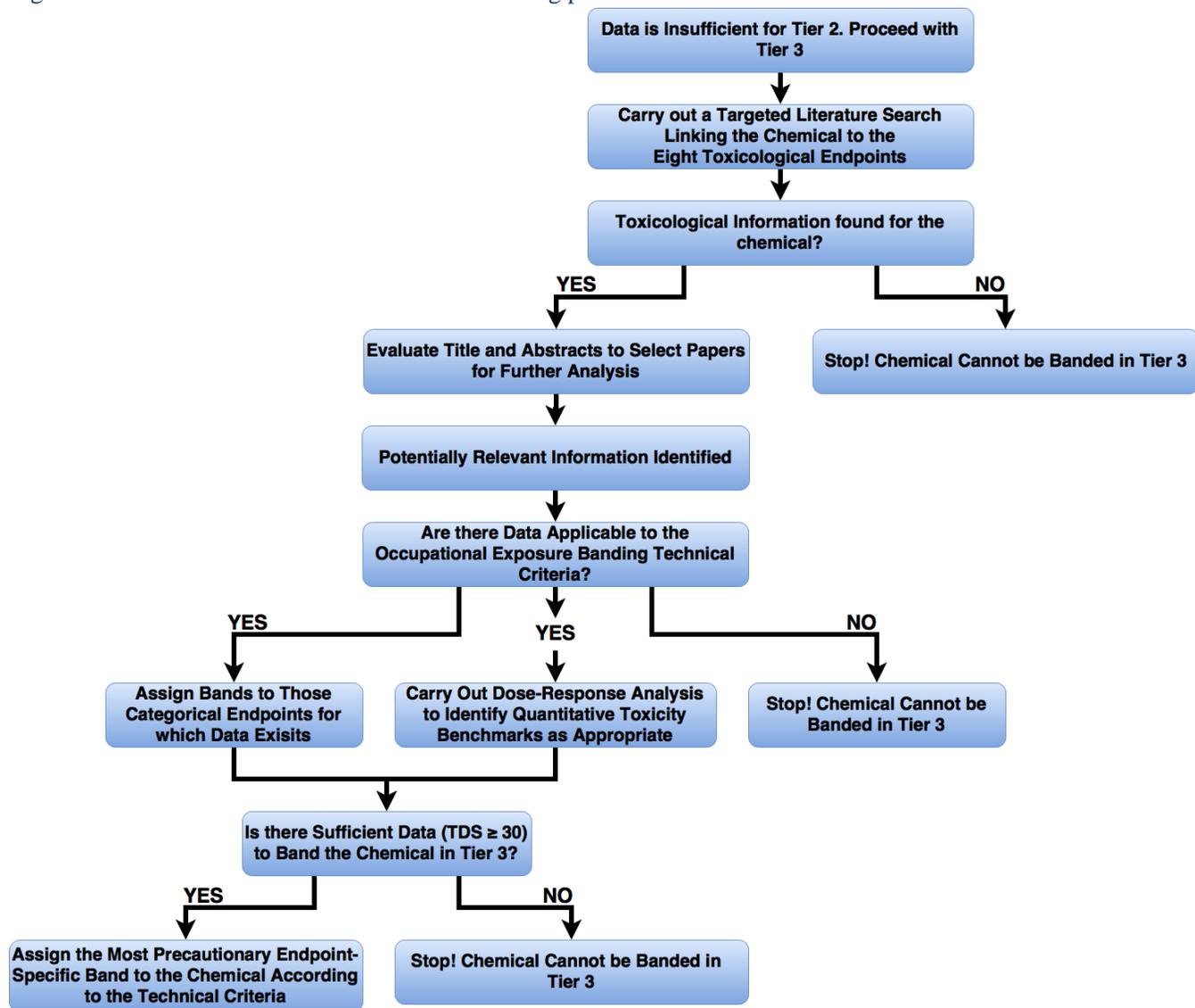
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## 1 Chapter 4 : Tier 3 Occupational Exposure 2 Banding: Using Expert Judgment to Evaluate 3 Experimental Data

4 The overall concept of the NIOSH occupational exposure banding process is the employment of  
5 simple procedures and clear rules for assigning chemicals to human health-related exposure  
6 bands. In Tier 1, this is based on information abstracted from GHS. In Tier 2, it is based on data  
7 summarized in authoritative secondary sources. However, the process recognizes that some  
8 chemicals may not be amenable to these processes because of insufficient information. If a user  
9 desires to scrutinize the potential human health impacts of a chemical beyond Tier 2, or when a  
10 TDS of 30 cannot be reached, further evaluation may require a detailed survey of the relevant  
11 primary literature and analysis of resulting experimental data on the nine primary toxicological  
12 effects that provide input to the occupational exposure banding process. These procedures should  
13 be done by, or in consultation with, persons with experience in evaluating experimental  
14 toxicological information.

15 Important elements of the Tier 3 process include (1) carrying out targeted electronic literature  
16 searches of bibliographic databases for research information and data on a chemical under  
17 consideration, (2) selecting studies of the chemical as they apply to the toxicological endpoints  
18 under consideration, (3) retrieving copies of appropriate articles from libraries or vendors, and  
19 (4) critically reading and evaluating the studies to discern the toxicological outcomes, including  
20 any available dose-response information. The latter information may provide a basis for deriving  
21 toxicity benchmarks such as NOAELs, LOAELs, SFs, and IURs. Derivation of one or more of  
22 these parameters is likely to be critical in assigning chemicals under evaluation to their most  
23 appropriate bands. To this end, the same outcome-specific technical criteria and determinant  
24 scores that apply to Tier 2 are used in Tier 3 for band selection and ensuring data sufficiency.  
25 This process is shown in Figure 4-1.

1 Figure 4-1: Flow chart for the Tier 3 hazard banding process



2

3

#### 4 4.1 Tier 3 Procedures

##### 5 Searching the Literature

6 It is recommended that a readily available gateway such as PubMed  
 7 (<http://www.ncbi.nlm.nih.gov/pubmed>) be used to identify and access the relevant scientific  
 8 information. Simple search statements linking the chemical or its CAS No. to the appropriate  
 9 toxicological and human health outcomes should be constructed. The search should cover the  
 10 period from the year before the most recently published authoritative review to the present, or for  
 11 an unlimited period if there are no agency-sponsored documents covering the subject chemical.

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### 1 **Selecting Relevant Studies**

2 Titles and abstracts of all “hits” should be reviewed to evaluate whether any of the identified  
3 articles are likely to contain categorical and/or dose-response information on the toxicological or  
4 human health impacts of the chemical under investigation. All potentially relevant articles should  
5 be retrieved from libraries or purchased from vendors.

### 6 **Evaluating the Studies**

7 Expert judgment should be used while reading the studies to determine whether dose-response  
8 information on the appropriate toxicological outcomes is available. While the primary toxicity  
9 benchmark for banding is the NOAEL, persons examining the data may need to derive other  
10 appropriate benchmarks such as the LOAEL, BMDL, BMCL, or, for cancer incidence data, the  
11 SF or IUR. It is assumed that individuals carrying out the Tier 3 evaluation will be familiar with  
12 these procedures. Factors to consider include power, standard procedures, model, and limitations.  
13 In addition, evaluating the reliability of the toxicological data by use of procedures such as the  
14 Klimisch score should be considered.

15 In conducting an assessment, a method to differentiate study quality or reliability should be  
16 employed. Klimisch and colleagues [Klimisch et al. 1997] proposed such a method by the  
17 development of what is now called “Klimisch scores.”

- 18 • Studies that were carried out according to generally valid and/or internationally accepted  
19 testing guidelines (e.g., good laboratory practice) or in which the test parameters  
20 documented are based on a specific testing guideline (e.g., OECD testing guideline) are  
21 given a Klimisch score of 1. A study with a Klimisch score of 1 is considered to be  
22 “reliable without restriction.” Most such studies are conducted by contract laboratories  
23 for industry.
- 24 • Studies in which the test parameters documented do not totally comply with the specific  
25 testing guideline, but are sufficient to accept, are given a Klimisch score of 2. These are  
26 studies that were probably not performed under good laboratory practice conditions and  
27 did not follow an internationally verified testing guideline (e.g., OECD), but which are  
28 nevertheless well documented and scientifically acceptable. Most of these studies are  
29 conducted by academia and are considered “reliable with restriction.”
- 30 • According to Klimisch et al. [1997], “studies or data from the literature/reports in which  
31 there are interferences between the measuring system and the test substance or in which  
32 organisms/test systems were used which are not relevant in relation to the exposure (e.g.,  
33 unphysiologic pathways of application) or which were carried out or generated according  
34 to a method which is not acceptable, the documentation of which is not sufficient for an  
35 assessment and which is not convincing for an expert judgment” are given a Klimisch  
36 score of 3 and are considered to be “not reliable.”
- 37 • Studies or data from the literature that do not give sufficient experimental details and that  
38 are only listed in short abstracts or secondary literature (e.g., books and reviews) are  
39 given a Klimisch score of 4 and considered “not assignable.”

## DRAFT

### 1 **Selecting a Band**

2 Derived toxicity benchmarks such as the NOAEL and any others mentioned above where  
3 applicable, should be compared to the relevant Tier 2 technical criteria for each toxicological  
4 endpoint. As before, the most health-protective band within and among endpoints should be  
5 selected as the overall band.

### 6 **Judging Data Sufficiency**

7 Information availability on the toxicological endpoints of interest provides critical input on data  
8 sufficiency in a similar manner to that described for Tier 2. The existence of data on a particular  
9 endpoint (for example, reproductive/developmental toxicity) contributes to a determinant score  
10 which, when combined with those available for other endpoints, should meet or exceed the TDS  
11 threshold of 30 out of a possible 125 (if all endpoints were represented). Failure to achieve a  
12 TDS of 30 would suggest that the chemical cannot be banded beyond the default within the  
13 NIOSH process.

### 14 **Assessing Uncertainty**

15 In a similar manner to the Tier 2 evaluation, it is recognized that the TDS addresses the range of  
16 toxicological endpoints that are identified for a particular compound but not the *number* of  
17 studies within each toxicological category. Given the higher degree of certainty potentially  
18 associated with multiple studies of each endpoint, it is likely that varying degrees of certainty on  
19 band selection will be determined for chemicals where the TDS is above the threshold for  
20 sufficiency. Users should also be aware that certainty can also be reduced when study results  
21 don't agree. Incorporating procedures such as the Klimisch scores may help address this issue.

# Chapter 5 : Special Issues in Occupational Exposure Banding

## 5.1 Impacts of Physical Form on OEB Selection

### OEBs and Associated OEL Ranges

After arraying the hazard data for each endpoint, the appropriate overall OEB for the chemical is determined considering all endpoints together. Each of the bands is associated with a range of exposure concentrations that serves as potential exposure control targets or as an exposure concentration range. Note that the concentration ranges are provided for additional context for the bands to support for their application in risk management decision making. The ranges reflect likely values for a health-based OEL given similar health hazard. However, the OEL ranges are designed only as a potential exposure control ranges. While it is most protective to keep exposures below the lower bound of the OEB, the actual control target could reflect any value in the range or other values based on other risk management considerations. These considerations include the level of confidence in the data set, the margin of safety associated with the specific exposure scenario being assessed, and the consequences of selecting an exposure control target that leads to control strategies that are insufficient or more than adequate.

### Selecting the OEL Range Category

Two possible OEL ranges are associated with each band, reflecting the need for exposure control ranges that differ for chemicals in different physical forms. Guidelines for selecting the OEL range category are as follows:

- The OEL range for bands for exposures to chemicals that are present in the form of gases or liquids that can form vapors in the occupational environment is provided in units of parts per million (ppm).
- The OEL range for bands for exposures to chemical that are present in the form of solid particles is provided in units of  $\text{mg}/\text{m}^3$ .
- Some chemicals that are liquids at standard temperature and pressure have sufficiently low vapor pressures that occupational exposure can occur in both the particulate phase (as liquid aerosols) and vapor phase. Such chemicals should generally be compared to the OEL range category for gas/vapor phase exposures (see details below).
- The OEL ranges for each band are specific to each physical form and were evaluated against health-based OELs for chemicals of similar physical characteristics; thus, gas or vapor phase chemicals **should not be converted** to units of  $\text{mg}/\text{m}^3$  for OEL range selection. Rather the OEB is determined first, and the related OEL range corresponding to that band is provided in the NIOSH occupational exposure banding process.

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### 1 OEL Range Concentrations Differ by Physical Form

2 The values of the OEB concentration ranges were developed on the basis of experience in field  
3 application of hazard banding processes and evaluation against existing OEL databases. The  
4 need for different OEL concentration ranges by physical form is based on the observation that  
5 the distribution of OELs for gases and vapors is shifted to higher concentrations when compared  
6 to particles when both forms are represented in units of  $\text{mg}/\text{m}^3$ . For example, a relatively low  
7 potency chemical vapor such as acetone has a NIOSH REL of 250 ppm ( $590 \text{ mg}/\text{m}^3$ ). In the  
8 context of controlling exposure to particulate exposures, a concentration of  $590 \text{ mg}/\text{m}^3$  is well  
9 above the allowable limit for even inert solid particles, which often have OELs in the range of 1  
10 to  $10 \text{ mg}/\text{m}^3$ . Note that the distributions do overlap, and thus clearly some vapors are more  
11 potent than some particles on an  $\text{mg}/\text{m}^3$  basis.

12 Certain respiratory tract physiological mechanisms might explain this difference in relative  
13 potency distributions on an  $\text{mg}/\text{m}^3$  basis for gases and vapors when compared to particulates  
14 [Oberdörster 1988; EPA 1994; Oberdorster 1995].

- 15 • An upper bound limit on exposures to solid particulates relates to physical mechanisms in the  
16 lung for overloading of normal particle clearance. This particle overload phenomenon caps  
17 the potency distribution for particles, but is not relevant for gases and vapors.
- 18 • Many toxic chemicals exert their effects at the level of the tissue response on the basis of  
19 local tissue dose. Thus, for a given total mass of chemical inhaled, the larger the surface area  
20 contacted, the lower the tissue concentration of the chemical at any single tissue location.  
21 Thus, for soluble particles, the local tissue dose can be higher for a given total exposure due  
22 to high deposition site doses compared to gases and vapors that are governed by dose  
23 diffusion.
- 24 • For insoluble particles overall respiratory tract retention time is often higher than for gases  
25 and vapors. To the degree that such particles induce a toxic response, the cumulative dose  
26 (reflecting local dose and amount of time the tissue is exposed) can be higher for solid  
27 particles compared to gases and vapors.
- 28 • The relative biological activity of low vapor pressure liquids is complex because such  
29 chemicals have properties that are intermediate between gases and solid particles. On the  
30 basis of analysis of health-based OELs for such low vapor pressure liquids, the OEB ranges  
31 identified on the basis of the NIOSH process generally align best with the vapor phase. This  
32 might reflect that such liquids dissolve in fluid layers of the respiratory tract and generally  
33 act more like vapors than solid particles in terms of clearance and local tissue doses.  
34 However, the less soluble and lower the vapor pressure the more like a solid particle such  
35 liquids will act. For liquids at the extreme end of the range for such properties both OEL  
36 range categories can be evaluated with recommendations to apply the band that is the most  
37 protective one recommended because liquids at either extreme may have properties that more  
38 closely resemble that of either gases or solids. Such evaluations could occur as part of an  
39 expert evaluation through a Tier 3 assessment.

1 To avoid the confusion in these differences by physical form, the occupational exposure banding  
2 process uses ppm as the preferred concentration units for gases/vapors. For solid particles, the  
3 bands are based on mg/m<sup>3</sup>.

## 4 **5.2 Mixed Exposures**

### 5 **Introduction**

6 Workers from agriculture, construction, mining and other industries are commonly exposed to  
7 combinations of chemicals, biological or physical agents, and other stressors. However,  
8 knowledge is limited about potential health effects from mixed exposures. Research has shown  
9 that physiological interactions from mixed exposures can lead to an increase in severity of the  
10 harmful effect. For example, exposure to noise and the solvent toluene results in a higher risk of  
11 hearing loss than exposure to either stressor alone. Exposure to both carbon monoxide and  
12 methylene chloride produces elevated levels of carboxyhemoglobin, reducing the blood's ability  
13 to carry oxygen in our bodies. Managing mixed exposures is a complex issue, given the large  
14 number of combinations that occur every day in a variety of workplaces and in our everyday life  
15 experiences.

### 16 **History**

17 Over the years NIOSH has published RELs for various mixed exposures within criteria  
18 documents and current intelligence bulletins. The process applied for mixed exposures has been  
19 unique depending upon the mixed exposures involved, state of the science, the policies employed  
20 at the time, and potential health effects. In the first decade of the National Occupational Research  
21 Agenda (NORA), the NORA Mixed Exposures Team was established to facilitate the study of  
22 occupational mixed exposures. In December, 2004, the NORA Mixed Exposures Team  
23 published a report based on its examination of the literature and ongoing research [NIOSH  
24 2004]. The report is a useful roadmap for understanding the complexity of dealing with mixed  
25 exposures. It identified the issues involved and research needed to appropriately handle  
26 occupational exposures to mixtures.

### 27 **Development of OEBs for Mixed Exposures [NRC 2009]**

28 Few mixed-exposure OELs have been established because assessment methods for mixed  
29 exposures have been based on extrapolation rather than direct toxicological data [Mumtaz et al.  
30 1995]. The current challenge for environmental and occupational scientists is to provide a sound,  
31 scientific basis that enables policymakers to substitute current, simplistic, single chemical  
32 standard setting with real-life, mixture-oriented standard setting [Feron et al. 1995]

33 Given the complexity of mixed exposures, multiple processes are needed to sample and assess  
34 exposure and risk. The current state of knowledge does not provide a basis for proposing a single

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1 process for risk assessment of mixed exposures. Several methodologies may be considered,  
2 including but not limited to the following processes:

### 3 *Whole-Mixture Process (Mixture Treated as a Single Toxic Agent) [NIOSH 2004]*

4 Whole-mixture testing considers the mixture as a single entity and conducts a standard health  
5 risk assessment for the chemical mixture in the same way that one is conducted for a single  
6 chemical. It is the simplest way to study the effects of a mixture, because the sole information  
7 needed to apply this process is the dose-response curve of the whole mixture in the organism  
8 desired.

### 9 *Similar-Mixture Process [NIOSH 2004]*

10 The similar-mixture process uses data on a well-studied, but toxicologically similar mixture to  
11 estimate the risk from the mixture. Mixtures are usually judged to be toxicologically similar on  
12 the basis of composition or observed toxicological properties.

### 13 *Group of Similar-Mixtures Process [NIOSH 2004]*

14 In the similar-mixtures process or comparative-potency method approach, the human toxicity of  
15 the mixture is estimated from that mixture's toxicity in a nonhuman study by multiplying by a  
16 proportionality constant that is estimated from data on the other mixtures.

### 17 *Component-Based Mixture Processes [NIOSH 2004]*

18 A single component of a chemical mixture may be a relevant index of toxicity when that  
19 component is suspected to account, qualitatively and quantitatively, for most of the toxicity. This  
20 process is useful, under the appropriate conditions, because only the dose-response information  
21 for the indicator is required. This method should only be used when synergy is not expected or  
22 known.

23 Special consideration should be given when banding chemicals comprised of a mixture of two or  
24 more chemicals. If health effect literature for the mixture exists, it should be used to band the  
25 chemical. If health information does not exist for the mixture, practitioners will band each  
26 chemical constituent independently in order to conduct OEBs for mixtures exposures. The  
27 resulting bands from chemical constituents will then be compared, and the most protective band  
28 will be selected for the mixture.

29 Employees may also be exposed to several individual chemicals at the same time in the  
30 workplace. In these situations, the OEBs should be conducted independently by chemical. These  
31 bands will be considered chemical by chemical in this mixed exposure. Care should be taken to  
32 determine if there are any synergistic effects of the mixed exposure.

## Chapter 6 : Preliminary Evaluation of Tier 1 and Tier 2 Protocols

Accuracy and usability of the NIOSH Occupational Exposure Banding Criteria are important to the success of the process. In order to evaluate the occupational exposure banding decision logic, NIOSH answered the following questions:

- Do the banding criteria reflect toxicity as determined by an independent evaluation (e.g., OELs)?
- Are the banding criteria consistent and specific when applied by independent users?
- Are some health effect endpoints more reliably banded than other health effects?

These evaluations provide additional confidence that the tool can be used effectively and consistently by stakeholders.

### 6.1. Evaluation of Tier 1 Criteria

Although NIOSH does not recommend banding chemicals with existing OELs, they are potential indicators of health hazard and potency. To evaluate the Tier 1 process, NIOSH compared the OELs of 804 chemicals to the Tier 1 OEBs for the same chemicals. OELs are not a perfect standard for comparison; however, they represent the current level to which chemical hazards are controlled. The chemicals selected for this exercise are all chemicals that have been assigned at least one full shift OELs, including NIOSH RELs, OSHA PELs, Cal/OSHA PELs, German MAKs, ACGIH TLVs, and AIHA WEELs.

During the evaluation, NIOSH determined whether the assigned OEB range included the existing OEL value for that chemical. The criterion for acceptance of the Tier 1 evaluation was that the assigned OEB would either contain the OEL or be more protective than the OEL for more than 80% of the chemicals. Based on other commonly used validation criteria, eighty percent was used rather than a lower percentage because the team determined it was the minimal level which provided confidence in the comparison. A higher percentage was not selected as it might diminish the usefulness of the OEB methodology. If the Tier 1 banding protocol was at least as protective as the OEL at least 80% of the time, this would demonstrate successful assignment of the GHS codes to OEBs. When more than one OEL was available for a substance, the lowest OEL was used for comparison. This step would further diminish bias that might be inherent to OELs based on the age for the OEL and the agency that it originated from. Table 6-1 below shows which type of OEL was utilized to conduct the comparisons. Note that the sum of sources in Table 6-1 is greater than 804 because nearly half the time the minimum OEL was the same value from 2 or more sources. The minimum OEL came from 2 sources 118 times, 3 sources 134 times, 4 sources 92 times and 5 sources 37 times.

1 **Table 6-1: Sources of OELs for the Tier 1 Evaluation exercise**

Source of minimum OEL	Frequency
TLV	448
MAK	204
WEEL	106
NIOSH REL	324
CAL PEL	356
OSHA PEL	176

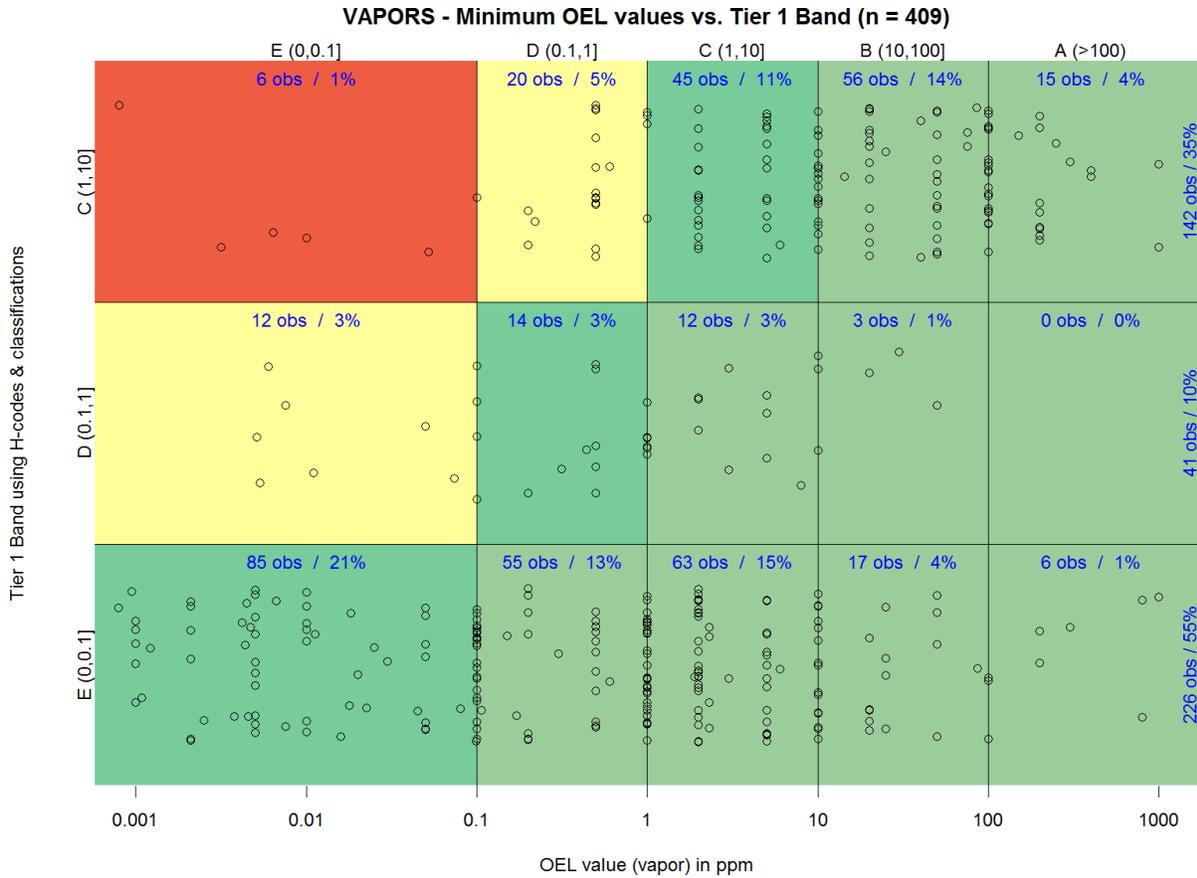
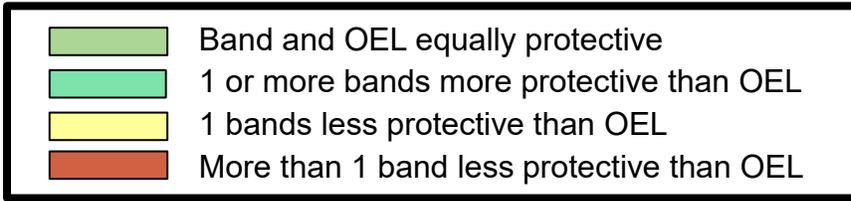
2 \* Sum is greater than 804 because the minimum OEL came from 2 or more sources 381 times.

3 NIOSH was able to retrieve GHS hazard codes and categories from the GESTIS database for 600  
 4 of the 804 chemicals. This data was used as the basis of our Tier 1 comparison. There were 409  
 5 gases/vapors and 191 dusts/particulates evaluated against the Tier 1 criteria based on GHS  
 6 hazard codes and categories.

7 In the figures below, the OEL on the x-axis is compared to the Tier 1 band on the y-axis. Each  
 8 circle on the figures represents an individual chemical. The color of the areas within the figure  
 9 represent the level of protection that the OEB offers compared to the OEL. For vapors (Figure  
 10 6-1), 91% of the chemicals were assigned a band in Tier 1 band that is at least as protective as  
 11 the OEL used for comparison. These chemicals fall within the green portion of the figure. For 32  
 12 of the 409 chemicals (8%), the Tier 1 band was one band less protective (shown in yellow) and  
 13 for 6/409 chemicals (1%), the Tier 1 band was two bands less protective (shown in red).

14  
 15  
 16  
 17  
 18

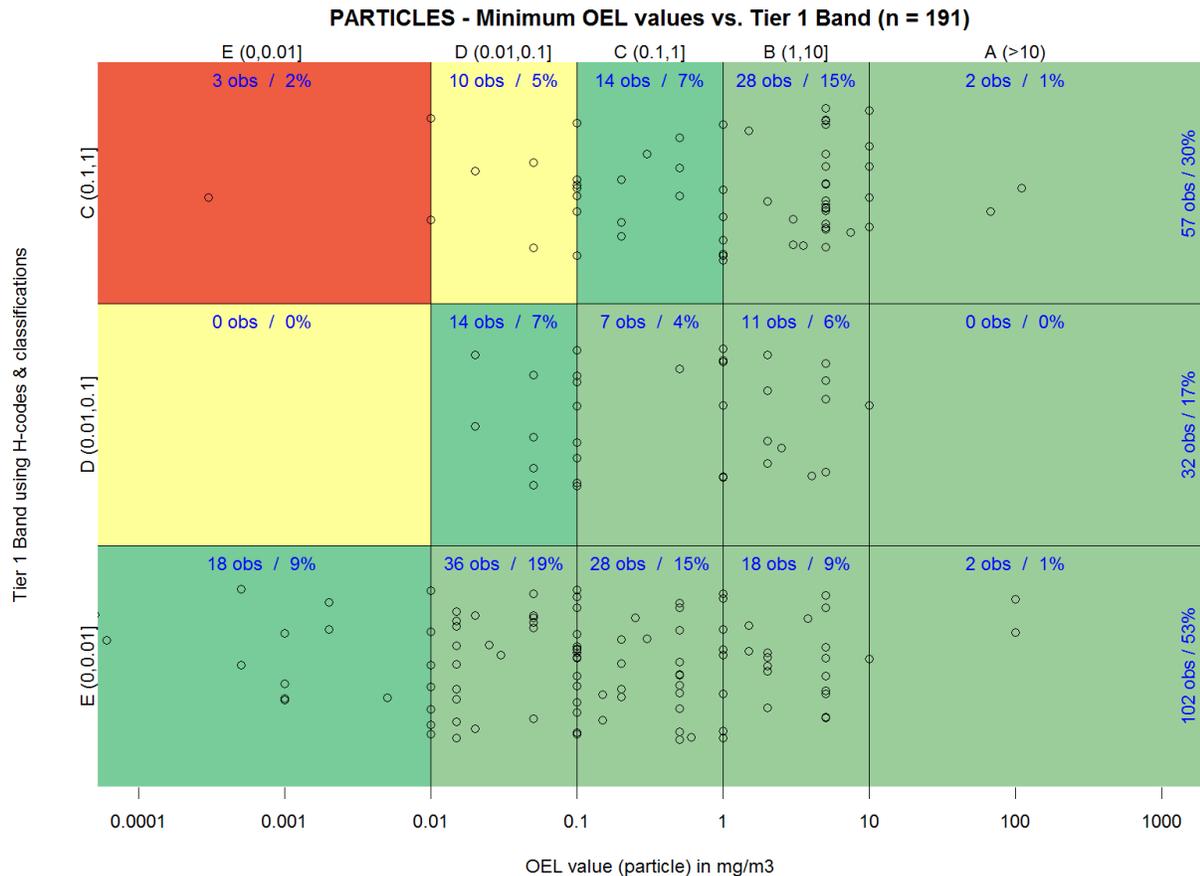
1 Figure 6-1: OEL values vs. Tier 1 band for vapors



3

4 For particles (Figure 6-2), 93% of the chemicals banded in Tier 1 were assigned a band that is at  
5 least as protective as the OEL used for comparison (shown in green). For 10/191 chemicals  
6 (5%), the band was one band less protective (shown in yellow) and for 3/191 substances (2%) of  
7 the time, the band was two bands less protective than the OEL (shown in red).

1 Figure 6-2: OEL values vs. Tier 1 Band for Particles



2

3 The overall agreement between the Tier 1 process and the derived OEBs exceeded the NIOSH a  
 4 priori hypothesis. This exercise provided confidence that chemicals banded with the Tier 1  
 5 process would be appropriately classified according to their potential to cause adverse health  
 6 effects. However, the process did not band chemicals with 100% accuracy. This may be due to  
 7 variability in how the OELs were set, policy decisions inherent within the creation of the OEL,  
 8 or new information reflected in either the OEL or limited information available to GHS hazard  
 9 code. Given this result, NIOSH recommends users to take advantage of the increased  
 10 information available in Tier 2 in order to increase the reliability of the banding and recommends  
 11 that the Tier 2 process be completed for all chemicals when user expertise and adequate data are  
 12 available.

1 **6.2. Evaluation of Tier 2 Criteria**

2 Tier 2 banding requires the user to access authoritative summary online information sources  
3 specified in the NIOSH criteria to assign a band for each health endpoint. There are quantitative  
4 criteria for some endpoints, such as LD<sub>50</sub> values for acute toxicity and the EPA IRIS inhalation  
5 unit risk value for cancer potency. Other endpoints, for example, genotoxicity, have qualitative  
6 criteria, such as “negative results,” “mixed results,” and “positive results.”

7 Sources of information are specific authoritative summaries of toxicity information. As an  
8 example, for carcinogenicity, the sources are: U.S. National Toxicology Program Report on  
9 Carcinogens, U.S. EPA IRIS, International Agency for Research on Cancer, Health Canada, and  
10 State of California Office of Environmental Health Hazard Assessment. The list of  
11 recommended sources for all 9 health endpoints are provided in Table 3-2.

12 Instructions are provided on how to evaluate the information in each source to determine an  
13 occupational exposure band. For example, if the inhalation unit risk calculated by U.S. EPA was  
14 0.002 per µg/m<sup>3</sup>, that would correspond with band D for cancer potency. See section 3.2 of the  
15 guidance document for complete details on the Tier 2 cancer evaluation. Sections 3.2-3.9 contain  
16 details on Tier 2 evaluation for all nine health endpoints.

17 Once all the sources for each health endpoint have been reviewed and the corresponding bands  
18 for each endpoint ascertained, the overall OEB is calculated, based on the bands derived from  
19 each endpoint and the TDS. The TDS is the sum of the endpoint determinant scores (EDS) that  
20 reflect the presence or absence of data on each endpoint, weighted to consider the most serious  
21 health endpoints more heavily. The final overall band is selected as the most health-protective  
22 endpoint band once a TDS of 30 is met. The exception to this is if one of the endpoint bands is  
23 band E in which case there is no threshold for the TDS. The details on data sufficiency and TDS  
24 can be found in section 3.0.

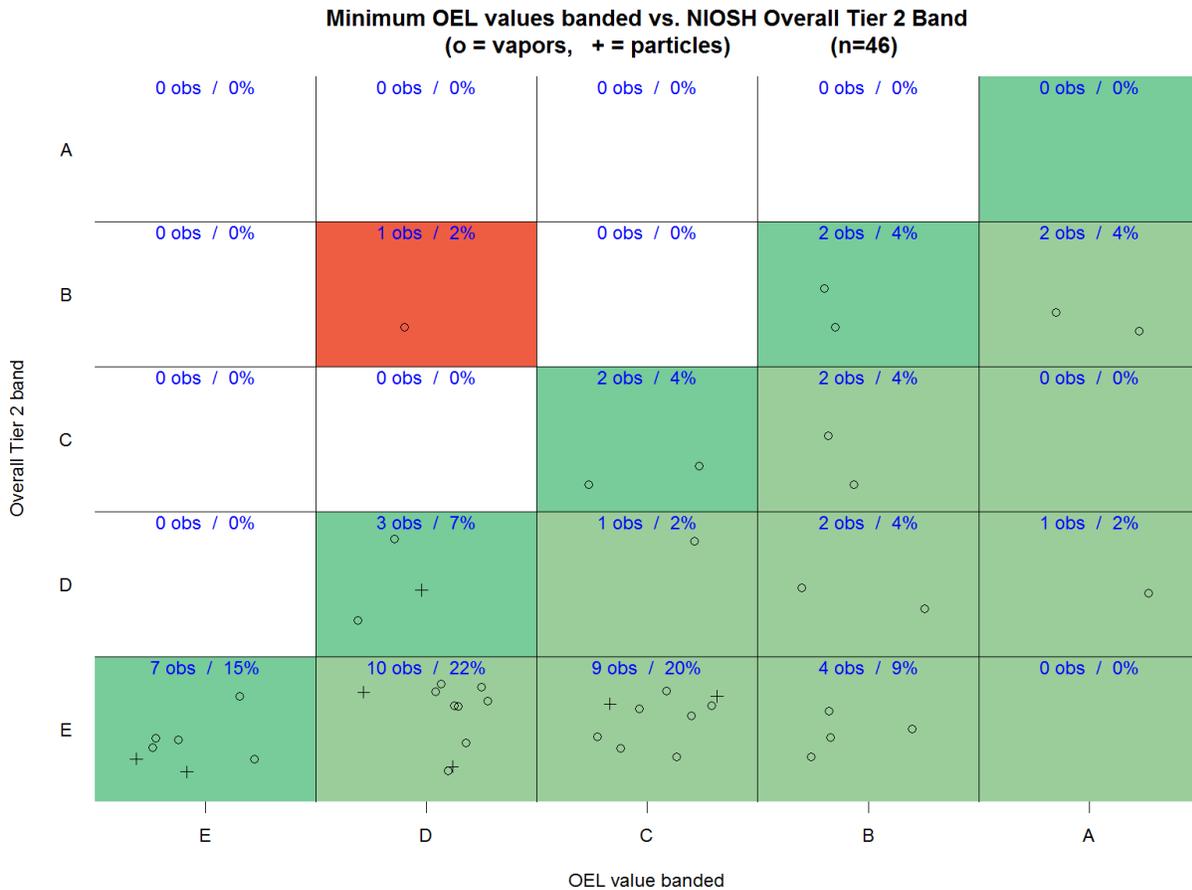
25 ***Comparison of Tier 2 Bands with OELs***

26 To evaluate the Tier 2 process, NIOSH compared the OELs of 53 chemicals to the Tier 2 OEBs  
27 for the same chemicals. This analysis was done similarly to the tier 1 evaluation. Although OELs  
28 are not a perfect standard for comparison, they represent the current level to which chemical  
29 hazards are controlled. To answer the question, “Do the banding criteria reflect toxicity as  
30 determined by an independent evaluation (e.g., OELs)?” Fifty three chemicals were banded by  
31 NIOSH users in the Tier 2 process and compared with existing OELs. NIOSH selected the  
32 chemicals from the EPA IRIS database, the TLV “Under Study” List, the MAK list of  
33 “Substances for which no MAK value can be established at present”, and chemicals listed on  
34 Health Canada. As in the Tier 1 comparison with OELs, the NIOSH target was to have the Tier 2  
35 band at least as protective as the OEL at least 80% of the time.

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1 In Figure 6-3, the band with the exposure range containing the OEL is displayed on the x-axis  
2 and is compared to the Tier 2 band on the y-axis. Of the 53 chemicals attempted, Tier 2 banding  
3 was completed for 46 chemicals. Of those 46 chemicals, the Tier 2 band was at least as  
4 protective as the OEL used for comparison (shown in green) for 45 chemicals (98%). For 1/46  
5 chemicals (2%), the band was two bands less protective than the OEL (shown in red). The 7  
6 chemicals that could not be banded in Tier 2 had OELs that fell in the range corresponding to  
7 band B (3 chemicals), band C (3 chemicals), and D (1 chemical).

8 Figure 6-3: Minimum OEL values banded vs. NIOSH overall Tier 2 band



9

10 **Comparison of Tier 1 and Tier 2 Banding Results**

11 Reviewers banded a sample of 53 of the original 804 chemicals in both Tier 1 and Tier 2. The  
12 target was that more than 80% of the time the Tier 1 band would be at least as protective as the  
13 Tier 2 band. Forty of those 53 chemicals had sufficient information to be banded in both Tier 1  
14 and Tier 2. One chemical could not be banded by either Tier 1 or Tier 2, six chemicals were  
15 banded in Tier 1 but sufficient information was not found to band them in Tier 2, and six

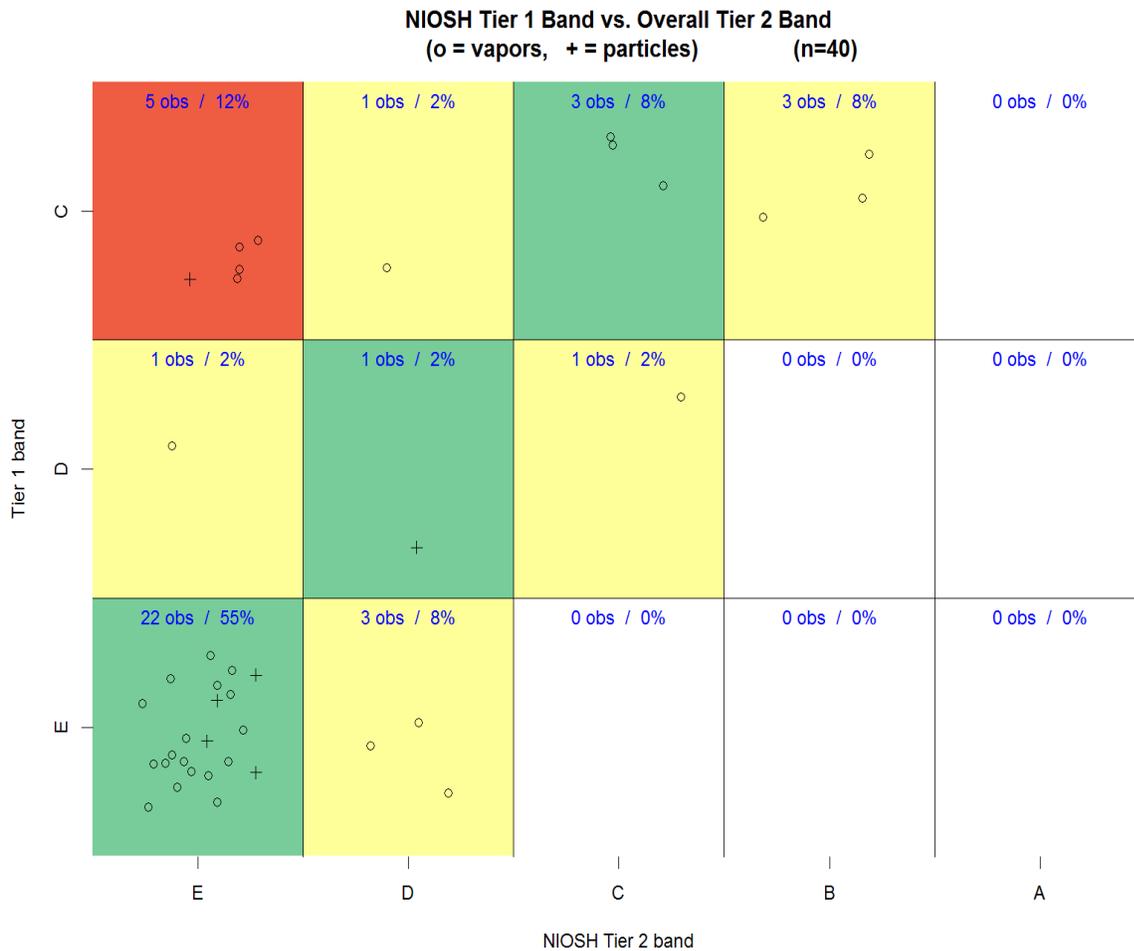
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1 chemicals that did not meet the criteria for banding in Tier 1 had sufficient information to band  
2 them in Tier 2. The results are shown in Figure 6-4. Twenty-six chemicals were assigned  
3 identical bands in Tier 1 and Tier 2. Nine chemicals had Tier 1 and Tier 2 bands that were one  
4 band different and five chemicals were banded 2 bands different.

5 For 65% of chemicals, there was perfect agreement between Tier 1 and Tier 2 bands. For 17.5  
6 percent of chemicals, Tier 1 is more protective than Tier 2. For another 17.5 percent, Tier 2 is  
7 more protective than Tier 1. Tier 1 is at least as protective as Tier 2 for 82.5% percent of the  
8 chemicals, which the initial target. These results further support our recommendation to always  
9 conduct a Tier 2 assessment.

10 **Figure 6-4: Comparison of Tier 1 vs. Tier 2 bands**

11



## DRAFT

### 1 *Evaluation of Tier 2 Criteria- Consistency*

2 Tier 2 criteria were evaluated for accuracy and usability by comparing the results across potential  
3 users. A total of 43 reviewers were recruited to evaluate the process. They were all occupational  
4 hygienists or had knowledge of occupational hygiene principles.

5 Each reviewer received 4 hours training developed by the NIOSH team. The amount of time  
6 required to teach and demonstrate the Tier 1 process to users was relatively short. Significantly  
7 more time was necessary to train users effectively on Tier 2. Each reviewer received two  
8 chemicals (Chemical 1 and Chemical 2), blank data sheets, and a copy of the banding criteria  
9 document. Reviewers emailed their results, and they were compiled anonymously. Of the  
10 recruited reviewers, 18 completed the full process and submitted banding information.

11 Tier 1 results (requested from half the reviewers) were identical for all reviewers for both  
12 chemicals. Tier 2 results (requested from all reviewers) showed that the overall band had much  
13 less variability than the individual endpoints. For Chemical 1, 12/16 found band D. One reviewer  
14 banded this chemical in band C, one in band E, and 2 in band B. One reviewer did not band this  
15 chemical and another did not complete the banding process. For Chemical 2, 12/18 banded this  
16 chemical in band E, and six banded it in band D.

17 Acute toxicity was the most consistent individual endpoint among reviewers who banded this  
18 endpoint, 13/17 and 14/18, assigning identical bands as shown in Figure 6-5 and Figure 6-6. The  
19 band assigned for other health endpoints showed had more variability. Reproductive toxicity  
20 responses ranged from band A to band E for Chemical 1 and from band A to band C for  
21 Chemical 2.

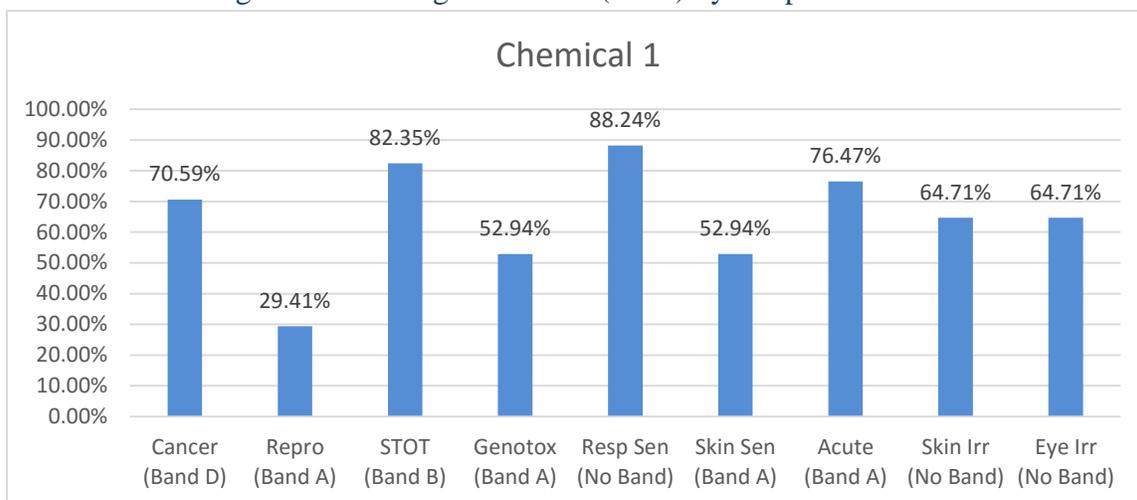
22 The total determinant score (measure of presence of data for each endpoint) varied across  
23 reviewers. For Chemical 1, the scores ranged from an insufficient 25 to 105, mean = 84 +/- 21.  
24 For Chemical 2, scores ranged from 40 to 110, mean = 83 +/-25. Results are presented in detail in  
25 Table 6-2 and Table 6-3.

26 **Table 6-2: Tier 2 Occupational Exposure Banding Results for Chemical 1 – 17 reviewers**

Chemical 1									
	Cancer	Repro	STOT	Genotox	Resp Sen	Skin Sen	Acute	Skin Irr	Eye Irr
A	1	5		9	2	9	13	1	2
B		2	14					4	4
C	1	4	2	5				1	
D	12	1							
E		1							
No Band	3	4	1	3	15	8	4	11	11
# of Users	17	17	17	17	17	17	17	17	17

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1 Figure 6-5: Percent Agreement among Reviewers (n=18) by Endpoint for Chemical 1

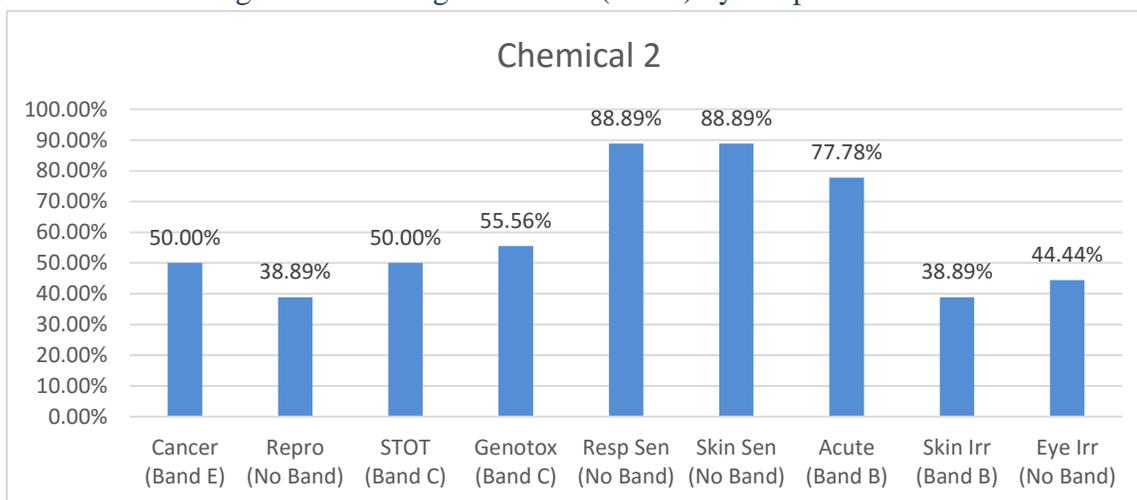


2

3 Table 6-3: Tier 2 Occupational Exposure Banding Results for Chemical 2 – 18 reviewers

Chemical 2									
	Cancer	Repro	STOT	Genotox	Resp Sen	Skin Sen	Acute	Skin Irr	Eye Irr
<b>A</b>		1		1	2	2			
<b>B</b>		6	1				14	7	4
<b>C</b>		4	9	10				5	6
<b>D</b>	8		3						
<b>E</b>	9		1	7					
<b>No Band</b>	1	7	4		16	16	4	6	8
<b># of Users</b>	18	18	18	18	18	18	18	18	18

4 Figure 6-6: Percent Agreement among Reviewers (n= 18) by Endpoint for Chemical 2



5

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1 NIOSH made comparisons between the results of the Tier 1 and Tier 2 process for these 2  
2 chemicals. For Chemical 1, the Tier 1 band and the Tier 2 band most reviewers selected were  
3 identical: band D. However, for Chemical 2, the Tier 1 band was C while most reviewers  
4 selected band E as the overall Tier 2 band.

5 Closer examination of the data for Chemical 2 indicate that the overall Tier 2 band was driven by  
6 the cancer and genotoxicity information. The H-codes for cancer are H350 and H351 while the  
7 H-codes for genotoxicity are H340 and H341. None of these H-codes are present in the GESTIS  
8 Substance Database so the Tier 1 band is driven by acute toxicity, skin irritation, and eye  
9 irritation which put Chemical 2 in band C. All but one reviewer located information on cancer  
10 for this chemical which puts the Tier 2 band into E. This reinforces the NIOSH recommendation  
11 to always complete the Tier 2 banding process. Stopping with a Tier 1 band is not recommended,  
12 since the H-codes may not be complete or as up-to-date as information found in the  
13 recommended data sources.

14 In a separate analysis, Tier 2 criteria were examined by four reviewers to assess accuracy and  
15 usability across chemicals for 20 additional chemicals. The chemicals were chosen by  
16 toxicologists because they were expected to have data across a wide range of health endpoints.  
17 In this exercise, each chemical was evaluated by 2 reviewers applying the Tier 2 criteria. Each  
18 of the four reviewers evaluated 10 chemicals. The reviewers had various levels of expertise,  
19 ranging from expert toxicologist and experienced industrial hygienist to Masters and Doctoral  
20 level public health students. They were given a copy of a draft banding document and blank data  
21 sheets. The users emailed their results, and they were compiled anonymously.

22 A comparison of the results from the reviewers is presented in Table 6-4. In this evaluation, the  
23 reviewers were in agreement 100% of the time for the tier 1 band. For the tier 2 evaluation, the  
24 reviewers were in agreement 60% for the overall band, and 75% of chemicals were banded  
25 within one band. When analyzing the individual endpoints, acute toxicity had the greatest  
26 agreement (80%) whereas genotoxicity had the least (20%). For endpoints that had lower  
27 agreement, a major cause of this is that one reviewer found information for a particular endpoint  
28 when the other reviewer did not. For example, for the genotoxicity endpoint, 55% of the time  
29 one reviewer found information to band a chemical when the other did not band for that endpoint  
30 at all.

31

32

33

## DRAFT

1 **Table 6-4: Occupational Exposure Banding Results for 20 Chemicals**

Endpoint	Comparison of Tier 2 Bands				
	Match	1 Band	2 Band	Band vs. No Band	Within One Band
Cancer	75%	15%	5%	5%	90%
Reproductive Toxicity	65%	15%	5%	15%	80%
STOT-RE	40%	25%	5%	30%	65%
Genotoxicity	20%	25%	0%	55%	45%
Respiratory Sensitization	50%	5%	5%	40%	55%
Skin Sensitization	40%	5%	0%	55%	45%
Acute Toxicity	85%	5%	10%	0%	90%
Skin Irritation	45%	45%	0%	10%	90%
Eye Irritation	35%	45%	10%	10%	80%
<b>Overall Band</b>	60%	15%	15%	10%	75%

2  
3 Banding results from these 20 chemicals were used to compare Tier 2 banding with the OELs.  
4 This is shown in Figure 6.7. The Tier 2 bands in this analysis were almost always at least as  
5 protective as the OEL. When the OEL for the chemical corresponded to band E (2 of the 20  
6 chemicals), the Tier 2 band was also E for both chemicals and both reviewers. The bands in  
7 those cases were driven by carcinogenicity (among other endpoints).

8 Of the 5 chemicals for which the OEL corresponded to band D, for 4 of the chemicals, at least  
9 one reviewer assigned band E, one reviewer selected band C for two of the chemicals and one  
10 reviewer did not locate information on the chemical for two chemicals. Health endpoints driving  
11 the banding included reproductive toxicity (1 chemical) and STOT-RE (2 chemicals). The  
12 remainder of chemicals were banded based on less quantitative endpoints such as genotoxicity,  
13 sensitization or irritation.

14 Of the 5 chemicals for which the OEL corresponded to band C, all were banded by both  
15 reviewers in band E. In two cases, one reviewer found information for the STOT-RE endpoint  
16 that drove the banding to band E. In all other cases, the banding was based on less quantitative  
17 endpoints such as genotoxicity, sensitization or irritation.

18 Of the 4 chemicals for which the OEL corresponded to band B, for one chemical neither  
19 reviewer found sufficient information to band the chemical in Tier 2. For the remaining 3

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1 chemicals, one reviewer selected band D for one chemical, the remainder were banded as band  
2 E. The health endpoint driving the bands for those three chemicals were primarily STOT-RE and  
3 cancer.

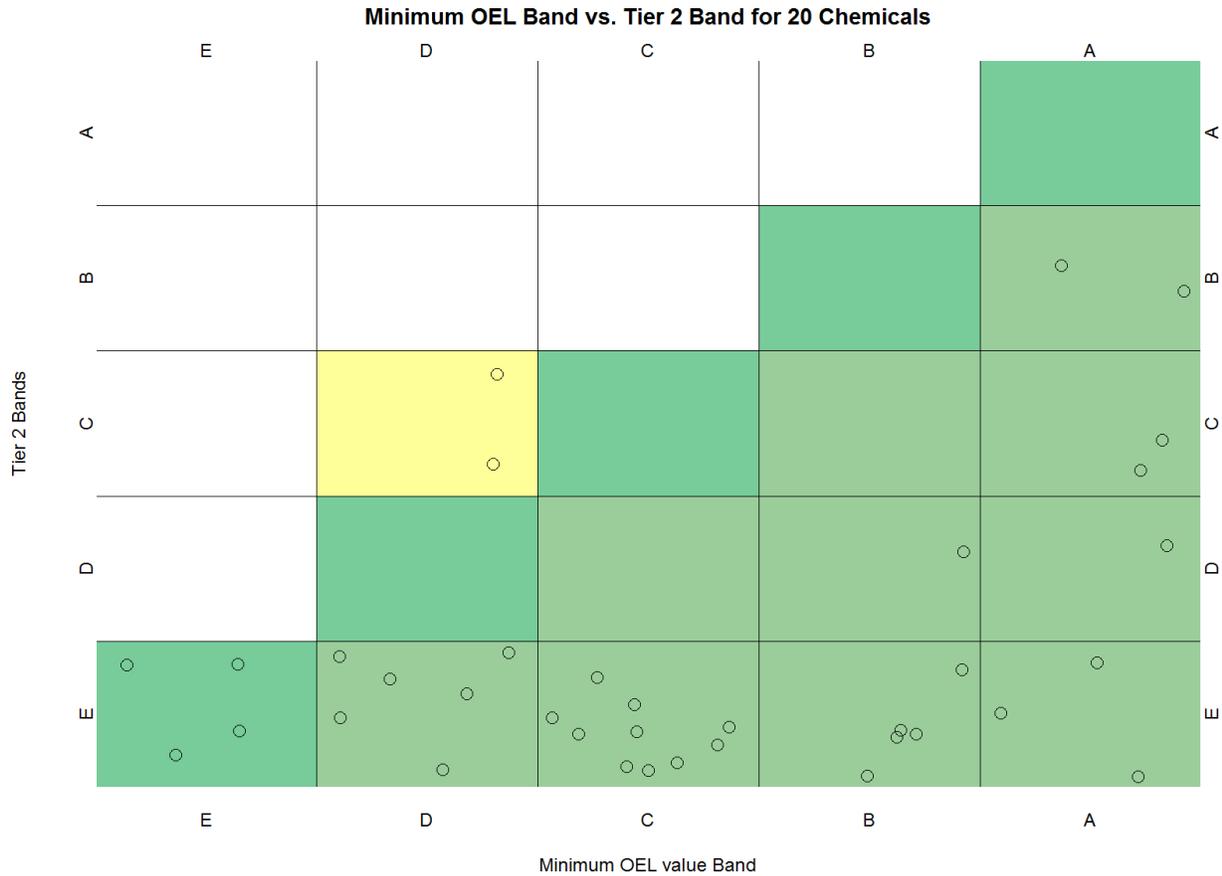
4 Of the 4 chemicals for which the OEL corresponded to band A, the reviewers tended to band the  
5 chemicals in more protective bands. None of the reviewers placed the chemicals in band A. The  
6 health endpoints driving these decisions appeared to be reproductive toxicity data in one case and  
7 STOT-RE, sensitization or irritation for the remainder. This may reflect the presence of more  
8 recent toxicity data than that which supported the OELs or the banding criteria may weight  
9 certain data types, such as irritation and sensitization data differently than an OEL setting  
10 process. In any case, the bands selected in the banding process for these chemicals were more  
11 protective than the OELs.

12 It is important to understand which endpoints drive the final band in order to assess whether the  
13 banding criteria is appropriate. There is higher confidence when the banding relies on the more  
14 quantitative endpoints, such as carcinogenicity, reproductive toxicity and STOT-RE. For the  
15 chemicals in this analysis, at times the band corresponding to the OEL suggested lower toxicity  
16 than the Tier 2 banding process. In those cases, frequently the band was supported by  
17 carcinogenicity data, reproductive toxicity data or data from STOT-RE. In those cases, rather  
18 than overprotection of the banding process, it may suggest that the OELs is under-protective for  
19 those endpoints. This may be the result of OELs set many years ago using different data or  
20 criteria than are accessible today. Further research on this point is warranted.

21 With regard to inter-user variability, there remains some variability in application of the banding  
22 process. Comparison of the banding results supports earlier analyses indicating that the acute  
23 toxicity, carcinogenicity and reproductive endpoints had the highest number of matches, while  
24 reviewers disagreed more frequently about genotoxicity data, eye-irritation and corrosion, and  
25 skin irritation and corrosion. When comparing Tier 2 bands to existing OELs for the 20  
26 chemicals, all but one chemical is more protective than existing OELs.

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- 1 Figure 6-7: Tier 2 Occupational Exposure Banding Results for 20 Chemicals (2 reviewers each)
- 2 Compared to Their Minimum OEL



3

4 **Discussion of Tier 2 Evaluation**

5 Since 2014, NIOSH has conducted a number of evaluation exercises to evaluate interrater  
6 reliability and overall agreement of the OEB methodology as well as refine the descriptions of  
7 the methodology in this document. A detailed analysis of the individual evaluations have been  
8 described above. A summary of evaluation activities primarily focusing on Tier 2 is presented in  
9 Table 6-5.

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1 **Table 6-5: Summary of Evaluation Activities for Tier 2**

<b>Evaluation Title</b>	<b>Phase 1 Evaluation</b>	<b>Phase 2 Evaluation</b>	<b>Phase 3 Evaluation</b>	<b>Phase 4 Evaluation</b>	<b>Phase 5 Evaluation</b>
<b>Time frame</b>	May-14	Sep-14	Jun-15	Sep-15	Oct-16
<b>Purpose</b>	To prototype training and conduct preliminary interrater reliability.	To conduct large scale banding effort and refine process.	To review endpoints results with interrater reliability.	To obtain additional data on Tier 2 endpoints to determine level of detail within endpoint descriptions.	To assess accuracy and usability across chemicals for additional chemicals.
<b>NIOSH Training class completed</b>	Yes	Yes	Yes	Yes	Yes
<b>Number of chemicals</b>	10	102	3	3	20
<b>Number of chemicals with OELs</b>	10	53	0	0	20
<b>Number of Reviewers</b>	9	10	43	18	4
<b>Tier 1 Evaluated</b>	Yes	No	Yes	Yes	Yes
<b>Tier 2 Evaluated</b>	Yes	Yes	Yes	Yes	Yes
<b>Lessons learned from Evaluation</b>	Some data source websites linked to another that had lesser quality.	Some endpoints such as skin sensitization needed more information.	Recruitment was easy, it was difficult to obtain completed information from reviewers. Learning curve was significant.	Confusion on TDS scoring in some cases.	Good agreement with endpoints based upon quantitative data.
<b>How OEB Methodology or Document Refined?</b>	Data sources curtailed to insure data quality	Materials with key sources were created. Skin sensitization endpoint documentation re-written.	Genotoxicity endpoint description was rewritten. Training on Tier 2 re-designed with example	TDS was streamlined and enhanced for clarity.	Endpoints based upon qualitative endpoints such as genotoxicity were further refined to aid in users finding information sources

2

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1 When analyzing the evaluation phases, key points can be identified as shown in Table 6-5. Other  
2 salient factors have also been highlighted which will be critical to OEB dissemination activities  
3 in the future. Users of Tier 2 must be well trained in how to use the NIOSH process.  
4 Discrepancies between users in selecting endpoint bands seem to be related to ability to locate  
5 data. In response, NIOSH has clarified the instructions to ameliorate this issue. Additionally,  
6 NIOSH has developed a training class with blended learning opportunities and is drafting a  
7 toxicology primer with skill-check questions to aid the process. This will better prepare users to  
8 understand the endpoints.

9  
10 The Tier 2 criteria operated as expected and the resulting bands showed overall consistency.  
11 Completing a Tier 2 evaluation requires substantial effort, not unlike other decision logics in  
12 occupational hygiene. Reviewers reported that banding a single chemical required hours to days.  
13 But this amount of time and effort is substantially less that what is required for a full quantitative  
14 risk assessment. The variability in TDS scores reflects that reviewers found different subsets of  
15 the available data, indicating differing levels of effort or expertise in navigating the sites. This  
16 may be less important for actual users who are highly motivated to evaluate their chemicals of  
17 interest.

18 For some endpoints, variability in the endpoint specific band between users existed. The  
19 variability in some endpoints appeared related to the clarity of the instructions and ease of use of  
20 the criteria. It is important that users read the occupational exposure banding process in its  
21 entirety before attempting to band chemicals. Compliance with this has been somewhat difficult  
22 to attain. The users often consulted training slides, rather than the full instructions, to more  
23 quickly use the banding process. Key details explained in the document were often missed by  
24 only using the training slides, and this created problems for users and is reflected in variability in  
25 the banding. This points to a need for a more streamlined and usable process. Given these  
26 observations, the guidance document was streamlined to enhance usability. In addition, an online  
27 tool is available to help facilitate the occupational exposure banding process. After each  
28 evaluation phase, enhancements have been made to the occupational exposure banding  
29 documentation and training materials, thereby improving the methodology. This process will  
30 continue as the document undergoes both external peer review, public and stakeholder comment.

31  
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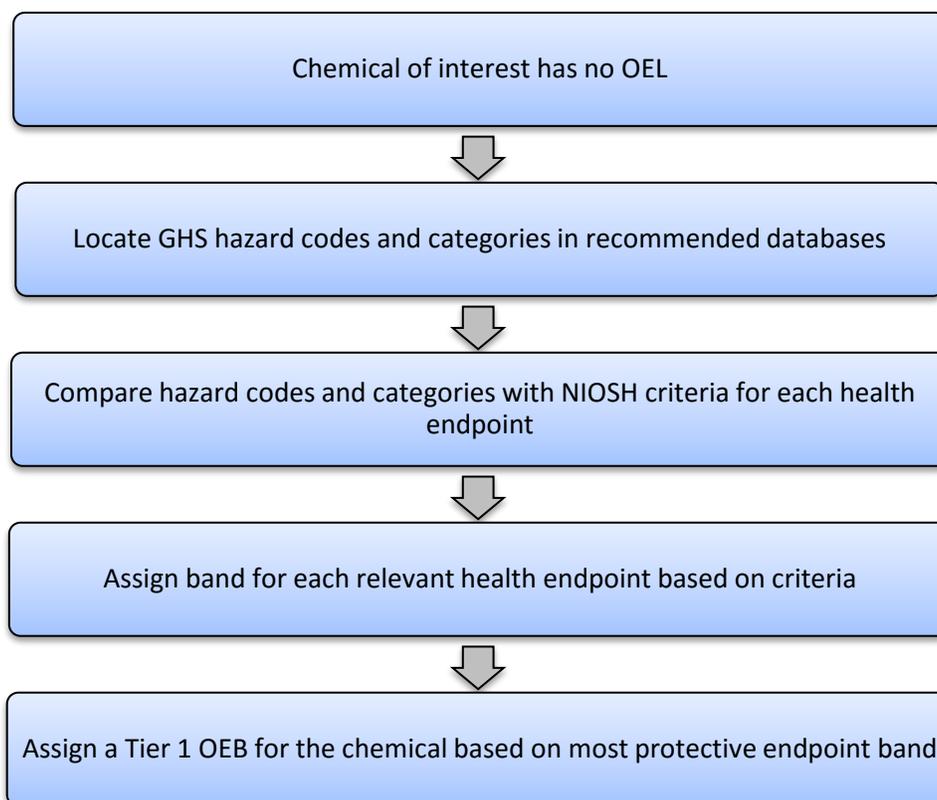
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# Appendix A: Helpful Information for Banding Chemicals in Tier 1

This Appendix provides supplemental information needed to band chemicals in Tier 1. Section A.1 gives a brief overview of the Tier 1 banding process. Section A.2 provides the NIOSH Tier 1 banding criteria. Once users gather the hazard codes and hazard categories necessary to complete Tier 1, they can then compare this data to the NIOSH criteria to determine an endpoint specific band. Hazard codes and categories can be retrieved from the GESTIS Substance Database, the Annex VI database, or a reliable OSHA-compliant SDS. Section A.3 provides the worksheet that can be filled out to keep a record of Tier 1 process. A web tool is also available to assist with this process: <https://www.cdc.gov/niosh/topics/oeb/default.html>. Refer to Chapter 1 of this guidance document for more specific details on conducting Tier 1 banding process.

## Section A.1 Tier 1 overview

### Tier 1 Overview



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**1 Section A.2 Tier 1 Criteria Overview: GHS Hazard Codes and Categories for Tier 1**

Preliminary NIOSH Tier 1 criteria		C	D	E
OEL ranges	Particle	> 0.1 to ≤ 1 milligrams per cubic meter of air (mg/m <sup>3</sup> )	> 0.01 to ≤ 0.1 mg/m <sup>3</sup>	≤ 0.01 mg/m <sup>3</sup>
	Vapor	> 1 to ≤ 10 parts per million (ppm)	> 0.1 to ≤ 1 ppm	≤ 0.1 ppm
Acute toxicity		H301 Category 3	H300 Category 2	H300 Category 1
		H302 Category 4		
		H331 Category 3	H330 Category 2	H330 Category 1
		H332 Category 4		
		H311 Category 3	H310 Category 2	H310 Category 1
		H312 Category 4		
				H314 Category 1, 1A, 1B, or 1C
				H318 Category 1
Respiratory and skin sensitization		H317 Category 1B (skin)	H317 Category 1 or 1A	—
		—	H334 Category 1B	H334 Category 1 or 1A
Germ cell mutagenicity		—	H341 Category 2	H340 Category 1, 1A or 1B
				H350 Category 1, 1A, or 1B
Carcinogenicity		—	—	H351 Category 2
		H361 (including H361f, H361d, and H361fd) Category 2	H360 (including H360f, H360d, and H360fd) Category 1B	H360 (including H360f, H360d, and H360fd) Category 1 or 1A
Specific target organ toxicity		H371 Category 2		H370 Category 1
		H373 Category 2	—	H372 Category 1

**2** Note that the following hazard codes will not be used for Tier 1 Banding: H200's, H303, H305, H313, H316, H320, H333, H335, H336,  
**3** H362, and H400's.

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1 **Section A.3 Tier 1 Worksheet**

2 This blank worksheet can be used to record hazard codes, hazard categories, the source of information,  
3 and the corresponding endpoint specific band based on the NIOSH criteria. The most protective of these  
4 bands is recorded at the bottom of the spreadsheet. This is the Tier 1 OEB for the chemical.

<b>Chemical Name:</b>					
<b>CAS:</b>					
<b>Endpoint</b>		<b>Hazard Code</b>	<b>Hazard Category</b>	<b>H-code Source</b>	<b>Endpoint Band</b>
<b>Acute Toxicity</b>	<b>Inhalation</b>				
	<b>Oral</b>				
	<b>Dermal</b>				
<b>Skin Corrosion/Irritation</b>					
<b>Eye Damage/Eye Irritation</b>					
<b>Respiratory and Skin Sensitization</b>					
<b>Germ Cell Mutagenicity</b>					
<b>Carcinogenicity</b>					
<b>Reproductive Toxicity</b>					
<b>Specific Target Organ Toxicity</b>					
<b>Most Protective Tier 1 Band</b>					

5 **Notes:**

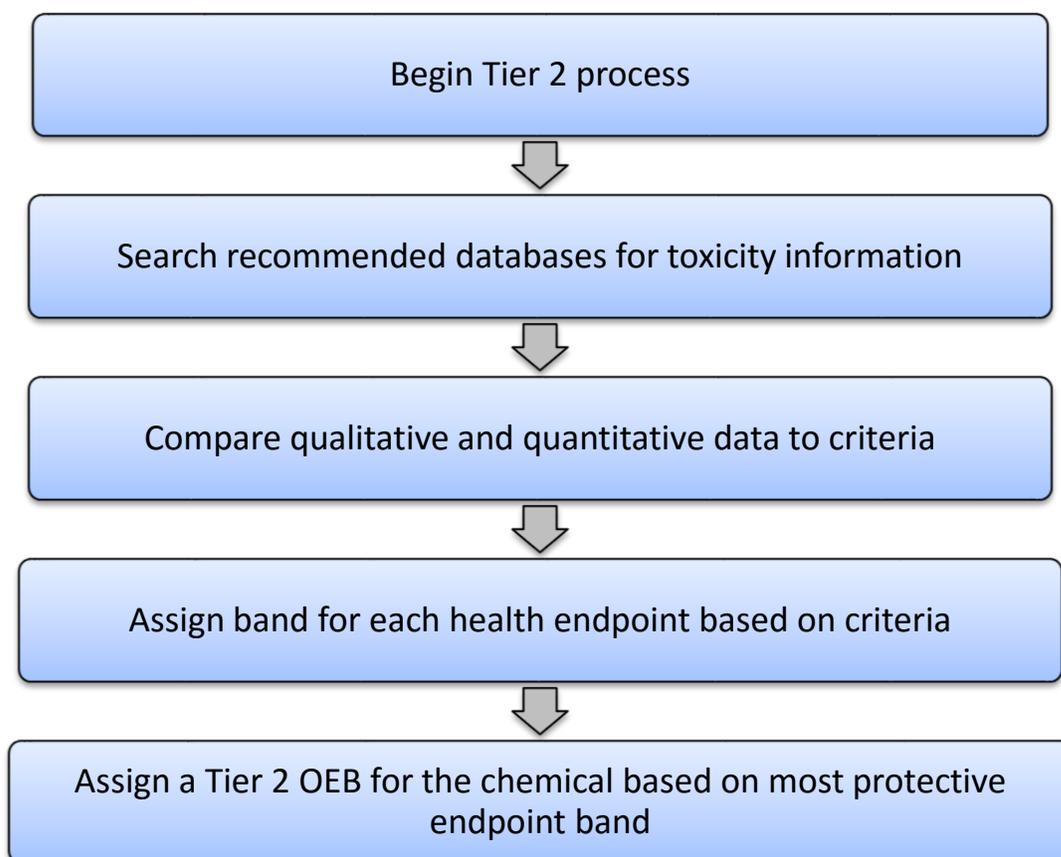
6

7

## 1 Appendix B: Helpful Information for Banding 2 Chemicals in Tier 2

3 This appendix provides supplemental information on banding chemicals in Tier 2. Section B.1 provides  
4 a brief overview of the Tier 2 banding process. Section B.2 provides a list of the assigned scores for  
5 each of the nine toxicological endpoints encountered in Tier 2 to determine the TDS. Section B.3  
6 provides a list of recommended data sources for each of the nine endpoints. Section B.4 provides a  
7 decision tree, data sources, NIOSH criteria, and a blank worksheet for each of nine endpoints, which can  
8 be used to band a chemical one endpoint at a time. Section B.5 provides a checklist that can be used to  
9 highlight the data that has been collected for each specific endpoint. A web tool is also available to assist  
10 with this process: <https://www.cdc.gov/niosh/topics/oeb/default.html>. Refer to Chapter 2 for more  
11 specific details on Tier 2 banding process.

### 12 Section B.1 Tier 2 Overview



13

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1 **Section B.2 Total Determinant Score: Assigned Scores for the Presence of Toxicological**  
2 **Endpoints Encountered in the Tier 2 Evaluation**  
3

<b>Toxicological Endpoint</b>	<b>Endpoint Determinant Score (EDS)</b>
Skin Irritation/Corrosion	5
Eye Irritation/Corrosion	5
Skin Sensitization	5
Acute Toxicity/Lethality (LD <sub>50</sub> or LC <sub>50</sub> )	5
Genotoxicity	5
Respiratory Sensitization	10
Systemic Target Organ Toxicity (STOT-RE)	30
Reproductive and Developmental Toxicity	30
Cancer WOE	20 or 30
Cancer SF, IUR, or TD/TC <sub>05</sub> (Health Canada)	30
<i>Endpoint Determinant Score for Cancer</i>	20 or 30
<b>Data Sufficiency/Total Determinant Score (TDS)</b>	30/125

4

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1 **Section B.3 Data Sources for Banding in Tier 2**

ENDPOINT	Rank	SOURCE OF INFORMATION*	ACRONYM
<b>Carcinogenicity</b>	1	<a href="#">U.S. National Toxicology Program Report on Carcinogens</a> [NTP-ROC 2016]	<a href="#">NTP-RoC</a>
		<a href="#">U.S. EPA Integrated Risk Information System</a> [EPA 2014]	<a href="#">IRIS</a>
		<a href="#">International Agency for Research on Cancer</a> [IARC 2015]	<a href="#">IARC</a>
		<a href="#">Health Canada</a> [Canada 1996]	<a href="#">HC</a>
		<a href="#">State of California Office of Environmental Health Hazard Assessment</a> [CAL/EPA 2010]	<a href="#">Cal OEHHA</a>
<b>Reproductive toxicity</b>	1	<a href="#">U.S. National Toxicology Program</a> [NTP 2016]	<a href="#">NTP</a>
		<a href="#">Health Canada</a> [Canada 1996]	<a href="#">HC</a>
		<a href="#">California Environmental Protection Agency</a> [CAL/EPA 2016]	<a href="#">CalEPA</a>
		<a href="#">Agency for Toxic Substances &amp; Disease Registry Toxicological Profiles</a> [ATSDR 2016]	<a href="#">ATSDR</a>
	2	<a href="#">Organization for Economic Co-operation and Development</a> [OECD 2016]	<a href="#">OECD</a>
		<a href="#">World Health Organization International Programme on Chemical Safety</a> [WHO-IPCS 2015]	<a href="#">WHO-IPCS</a>
		<a href="#">U.S. EPA Office of Pesticides: Reregistration Eligibility Decision Documents</a> [EPA 2016a]	<a href="#">U.S. EPA RED</a>
		<a href="#">European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals</a> [ECHA 2016]	<a href="#">ECHA; REACH</a>
<b>Specific Target Organ Toxicity (STOT-RE)</b>	1	<a href="#">Agency for Toxic Substances &amp; Disease Registry Toxicological Profiles</a> [ATSDR 2016]	<a href="#">ATSDR</a>
		<a href="#">U.S. EPA Integrated Risk Information System</a> [EPA 2014]	<a href="#">IRIS</a>
		<a href="#">California Environmental Protection Agency</a> [CAL/EPA 2016]	<a href="#">CalEPA</a>
		<a href="#">U.S. National Toxicology Program</a> [NTP 2016]	<a href="#">NTP</a>
		<a href="#">Health Canada</a> [Canada 1996]	<a href="#">HC</a>
	2	<a href="#">European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals</a> [ECHA 2016]	<a href="#">REACH</a>
		<a href="#">Organization for Economic Co-operation and Development</a> [OECD 2016]	<a href="#">OECD</a>
<b>Genotoxicity</b>	1	<a href="#">U.S. National Toxicology Program</a> [NTP 2016]	<a href="#">NTP</a>
		<a href="#">Agency for Toxic Substances &amp; Disease Registry Toxicological Profiles</a> [ATSDR 2016]	<a href="#">ATSDR</a>

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		<a href="#">U.S. National Toxicology Program Report on Carcinogens</a> [NTP-ROC 2016]	<a href="#">NTP-RoC</a>
		<a href="#">World Health Organization International Programme on Chemical Safety</a> [WHO-IPCS 2015]	<a href="#">WHO-IPCS</a>
	2	<a href="#">Hazardous Substance Data Bank</a> [HSDB 2016]	<a href="#">HSDB</a>
		<a href="#">European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals</a> [ECHA 2016]	<a href="#">REACH</a>
<b>Respiratory sensitization</b>	1	<a href="#">Organization for Economic Co-operation and Development</a> [OECD 2016]	<a href="#">OECD</a>
		<a href="#">European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals</a> [ECHA 2016]	<a href="#">REACH</a>
		<a href="#">World Health Organization International Programme on Chemical Safety</a> [WHO-IPCS 2015]	<a href="#">WHO-IPCS</a>
	2	<a href="#">Agency for Toxic Substances &amp; Disease Registry Toxicological Profiles</a> [ATSDR 2016]	<a href="#">ATSDR</a>
		<a href="#">U.S. EPA Integrated Risk Information System</a> [EPA 2014]	<a href="#">IRIS</a>
		<a href="#">Association of Occupational and Environmental Clinics</a> [AOEC 2016]	<a href="#">AOEC</a>
<b>Skin sensitization</b>	1	<a href="#">NIOSH Skin Notation Profiles</a> [NIOSH 2009b]	<a href="#">SK Profiles</a>
		<a href="#">European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals</a> [ECHA 2016]	<a href="#">REACH</a>
		<a href="#">Organization for Economic Co-operation and Development</a> [OECD 2016]	<a href="#">OECD</a>
		<a href="#">World Health Organization International Programme on Chemical Safety</a> [WHO-IPCS 2015]	<a href="#">WHO-IPCS</a>
	2	<a href="#">Hazardous Substance Data Bank</a> [HSDB 2016]	<a href="#">HSDB</a>
<b>Acute Toxicity</b>	1	<a href="#">National Library of Medicine ChemID Plus</a> [ChemID 2016]	<a href="#">ChemID Plus</a>
		<a href="#">U.S. EPA Superfund Chemical Data Matrix</a> [EPA 2016b]	<a href="#">U.S. SCDM</a>
		<a href="#">Pesticide Properties Database</a> [PPDB 2007]	<a href="#">PPDB</a>
		<a href="#">World Health Organization International Programme on Chemical Safety</a> [WHO-IPCS 2015]	<a href="#">WHO-IPCS</a>
	2	<a href="#">Hazardous Substance Data Bank</a> [HSDB 2016]	<a href="#">HSDB</a>
<a href="#">Agency for Toxic Substances &amp; Disease Registry Toxicological Profiles</a> [ATSDR 2016]		<a href="#">ATSDR</a>	
	1	<a href="#">NIOSH Skin Notation Profiles</a> [NIOSH 2009b]	<a href="#">SK Profiles</a>
		<a href="#">World Health Organization International Programme on Chemical Safety</a> [WHO-IPCS 2015]	<a href="#">WHO-IPCS</a>

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<b>Skin Irritation/Skin Corrosion</b>		<a href="#">European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]</a>	<a href="#">REACH</a>
		<a href="#">Organization for Economic Co-operation and Development [OECD 2016]</a>	<a href="#">OECD</a>
	2	<a href="#">Agency for Toxic Substances &amp; Disease Registry Toxicological Profiles [ATSDR 2016]</a>	<a href="#">ATSDR</a>
		<a href="#">U.S. EPA Integrated Risk Information System [EPA 2014]</a>	<a href="#">IRIS</a>
<b>Serious Eye Damage/Eye Irritation</b>	1	<a href="#">Organization for Economic Co-operation and Development [OECD 2016]</a>	<a href="#">OECD</a>
		<a href="#">World Health Organization International Programme on Chemical Safety [WHO-IPCS 2015]</a>	<a href="#">WHO-IPCS</a>
		<a href="#">European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals [ECHA 2016]</a>	<a href="#">REACH</a>
	2	<a href="#">Agency for Toxic Substances &amp; Disease Registry Toxicological Profiles [ATSDR 2016]</a>	<a href="#">ATSDR</a>
		<a href="#">U.S. EPA Integrated Risk Information System [EPA 2014]</a>	<a href="#">IRIS</a>

1 \*These links are up to date as of December 11, 2017.

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1 **Section B.4 Endpoint Specific Criteria for Banding**

2 *Cancer*

3 Data Sources

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Carcinogenicity	1	U.S. National Toxicology Program Report on Carcinogens	NTP-RoC
		U.S. EPA Integrated Risk Information System	IRIS
		International Agency for Research on Cancer	IARC
		Health Canada	HC
		State of California Office of Environmental Health Hazard Assessment	Cal OEHHA

4 Criteria for Carcinogenicity Toxicity (Quantitative Analysis)

NIOSH Banding Criteria for <b>Cancer</b>			
Exposure/ Dosing Route	Band		
	C	D	E
Slope factor	< 0.01 (mg/kg-day) <sup>-1</sup>	≥ 0.01 to < 10 (mg/kg-day) <sup>-1</sup>	≥ 10 (mg/kg-day) <sup>-1</sup>
Inhalation unit risk	< 3 × 10 <sup>-6</sup> (µg/m <sup>3</sup> ) <sup>-1</sup>	≥ 3 × 10 <sup>-6</sup> to < 0.01 (µg/m <sup>3</sup> ) <sup>-1</sup>	≥ 0.01 (µg/m <sup>3</sup> ) <sup>-1</sup>
TD <sub>05</sub>	> 5 mg/kg-day	> 0.005 to ≤ 5 mg/kg-day	≤ 0.005 mg/kg-day
TC <sub>05</sub>	> 16700 µg/m <sup>3</sup>	> 5 to ≤ 16700 µg/m <sup>3</sup>	≤ 5 µg/m <sup>3</sup>

5 Criteria for Carcinogenicity Toxicity (Qualitative Analysis)

Classification	Band	Determinant Score
<b>National Toxicology Program Report on Carcinogens</b>		
<i>Known to be human carcinogen</i>	<b>E</b>	<b>30</b>
<i>Reasonably anticipated to be human carcinogen</i>	<b>E</b>	<b>30</b>
<b>Environmental Protection Agency Integrated Risk Information System</b>		
<i>Group A (human carcinogen)</i>	<b>E</b>	<b>30</b>
<i>Carcinogenic to humans</i>	<b>E</b>	<b>30</b>
<i>Group B1 (probable human carcinogen)</i>	<b>E</b>	<b>30</b>
<i>Group B2 (probable human carcinogen)</i>	<b>E</b>	<b>30</b>
<i>Likely to be carcinogenic to humans</i>	<b>E</b>	<b>30</b>
<i>Group C (possible human carcinogen)</i>	<b>D</b>	<b>20</b>
<i>Suggestive evidence of carcinogenic potential</i>	<b>D</b>	<b>20</b>
<i>Group D (not classifiable as to human carcinogenicity)</i>	<i>No band</i>	<i>No score</i>
<i>Data are inadequate for an assessment of carcinogenic potential</i>	<i>No band</i>	<i>No score</i>
<i>Group E (evidence of non-carcinogenicity for humans)</i>	<b>A</b>	<b>30</b>
<i>Not likely to be carcinogenic to humans</i>	<b>A</b>	<b>30</b>
<b>International Agency for Research on Cancer</b>		

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<i>Group 1 (carcinogenic to humans)</i>	<b>E</b>	<b>30</b>
<i>Group 2A (probably carcinogenic to humans)</i>	<b>E</b>	<b>30</b>
<i>Group 2B (possibly carcinogenic to humans)</i>	<b>E</b>	<b>30</b>
<i>Group 3 (not classifiable as to its carcinogenicity to humans)</i>	<i>No band</i>	<i>No score</i>
<i>Group 4 (probably not carcinogenic to humans)</i>	<b>A</b>	<b>30</b>
<b>State of California Office of Environmental Health Hazard Assessment</b>		
<i>Type of toxicity = cancer</i>	<b>E</b>	<b>30</b>

1 **Worksheet for Cancer**

<b>Carcinogenicity (20 or 30 points possible)</b>				
	<b>Band A</b>	<b>Band C</b>	<b>Band D</b>	<b>Band E</b>
<b>NTP/EPA/IARC/Canada/California (QUALITATIVE)</b>				
<b>EPA IRIS Slope Factor</b>				
<b>EPA IRIS Inhalation Unit Risk</b>				
<b>Health Canada TD05</b>				
<b>Health Canada TC05</b>				
<b>California Slope Factor</b>				
<b>California Inhalation Unit Risk</b>				

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- 4
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1 *Reproductive Toxicity*

2 Data Sources

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
<b>Reproductive toxicity</b>	1	U.S. National Toxicology Program	NTP
		Health Canada	HC
		California Environmental Protection Agency	CalEPA
		Agency for Toxic Substances & Disease Registry Toxicological Profiles	ATSDR
	2	Organization for Economic Co-operation and Development	OECD
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
		U.S. EPA Office of Pesticides: Reregistration Eligibility Decision Documents	U.S. EPA RED
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	ECHA; REACH

3

4 Criteria for Reproductive Toxicity Endpoint

NIOSH Banding Criteria for <b>Reproductive Toxicity</b> (NOAEL/BMDL/BMCL)					
Exposure/ Dosing Route	Band				
	A	B	C	D	E
Oral, dermal	> 300 mg/kg-day	> 30 to ≤300 mg/kg-day	> 3 to ≤30 mg/kg-day	> 0.3 to ≤3 mg/kg-day	≤0.3 mg/kg-day
Inhalation (gases and vapors)	> 10,000 ppm	> 1,000 to ≤10,000 ppm	> 100 to ≤1,000 ppm	> 10 to ≤100 ppm	≤10 ppm
Inhalation (dusts and mists)	> 10,000 µg/m <sup>3</sup>	> 1,000 to ≤10,000 µg/m <sup>3</sup>	> 100 to ≤1,000 µg/m <sup>3</sup>	> 10 to ≤100 µg/m <sup>3</sup>	≤10 µg/m <sup>3</sup>

5 Worksheet for Reproductive Toxicity

<b>Reproductive Toxicity (30 points possible)</b>					
Data supports:	Band A	Band B	Band C	Band D	Band E
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.					
Source, Rank 1 or 2:					

6

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**DRAFT**

1 *Specific Target Organ Toxicity (STOT-RE)*

2

3 Data Sources

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Specific Target Organ Toxicity (STOT-RE)	1	Agency for Toxic Substances & Disease Registry Toxicological Profiles	ATSDR
		U.S. EPA Integrated Risk Information System	IRIS
		California Environmental Protection Agency	CalEPA
		U.S. National Toxicology Program	NTP
		Health Canada	HC
	2	European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
		Organization for Economic Co-operation and Development	OECD
		World Health Organization International Programme on Chemical Safety	WHO-IPCS

4

5 Criteria for Specific Target Organ Toxicity (STOT-RE) Endpoint

NIOSH Banding Criteria for Specific Target Organ Toxicity (NOAEL/BMDL)					
Exposure/ Dosing Route	Band				
	A	B	C	D	E
Oral, dermal	>1,000 mg/kg-day	>100 to ≤1,000 mg/kg-day	>10 to ≤100 mg/kg-day	>1 to ≤10 mg/kg-day	≤1 mg/kg-day
Inhalation (dusts and mists)	>30,000 µg/m <sup>3</sup>	>3,000 to ≤30,000 µg/m <sup>3</sup>	>300 to ≤3,000 µg/m <sup>3</sup>	>30 to ≤300 µg/m <sup>3</sup>	≤30 µg/m <sup>3</sup>
Inhalation (gases and vapors)	>30,000 ppm	>3,000 to ≤30,000 ppm	>300 to ≤3,000 ppm	>30 to ≤300 ppm	≤30 ppm

6 \* Multiple NOAELs for one chemical substance may be available. The NOAEL selected for banding should be the NOAEL used  
7 by the agency as the basis for the reference dose/concentration.

8 Worksheet for Specific Target Organ Toxicity – Repeated Exposure (STOT-RE) Endpoint

<b>Specific Target Organ Toxicity (STOT-RE) (30 points possible)</b>					
Data supports:	Band A	Band B	Band C	Band D	Band E
If data available, put data, notes, etc. in this row corresponding to the correct band criteria; otherwise leave blank.					
Source, Rank 1 or 2:					

**DRAFT**

1 *Genotoxicity*

2 Data Sources

<b>ENDPOINT</b>	<b>Rank</b>	<b>SOURCE OF INFORMATION</b>	<b>ACRONYM</b>
<b>Genotoxicity</b>	1	U.S. National Toxicology Program	NTP
		Agency for Toxic Substances & Disease Registry	ATSDR
		U.S. National Toxicology Program Report on Carcinogens	NTP-RoC
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
	2	Hazardous Substance Data Bank	HSDB
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH

3 Criteria for Genotoxicity Endpoint

<b>NIOSH Banding Criteria for Genotoxicity</b>		
<b>Band</b>		
<b>A</b>	<b>C</b>	<b>E</b>
Negative Results	Mixed results	Positive Results

4 Worksheet for Genotoxicity

<b>Genotoxicity (5 points possible)</b>			
<b>Data supports:</b>	<b>Negative Results (Band A)</b>	<b>Mixed Results (Band C)</b>	<b>Positive Results (Band E)</b>
<b>If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.</b>			
<b>Source, Rank 1 or 2:</b>			

- 5
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**DRAFT**

1 *Respiratory Sensitization*

2 Data Sources

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
<b>Respiratory sensitization</b>	1	Organization for Economic Co-operation and Development	OECD
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
	2	Agency for Toxic Substances & Disease Registry	ATSDR
		U.S. EPA Integrated Risk Information System	IRIS
		Association of Occupational and Environmental Clinics	AOEC

3 Criteria for Respiratory Sensitization Endpoint

NIOSH Banding Criteria for <b>Respiratory Sensitization</b>		
Band		
A	C	E
No evidence of respiratory sensitization	Mixed results	Positive evidence of respiratory sensitization

4 Worksheet for Respiratory Sensitization Endpoint

<b>Respiratory sensitization (10 points possible)</b>			
Data supports:	No evidence of respiratory sensitization (Band A)	Mixed results (Band C)	Respiratory sensitization based on totality of evidence (Band E)
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.			
Source, Rank 1 or 2:			

5  
6  
7  
8

**DRAFT**

1 *Skin Sensitization*

2 Data Sources

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Skin sensitization	1	NIOSH Skin Notation Profiles	SK Profiles
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
		Organization for Economic Co-operation and Development	OECD
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
	2	Hazardous Substance Data Bank	HSDB

3 Criteria for Skin Sensitization Endpoint

NIOSH Banding Criteria for Skin Sensitization			
Test Type	Band		
	A	C	E
EC3 (%) (based on LLNA)	Non-skin sensitizer	EC3 (%) $\geq 2.0 \leq 100$ (weak to moderate skin sensitizer)	EC3 (%) $\leq 2.0$ (strong to extreme skin sensitizer)
GPMT	No positive response or low incidence data	30% to 60% responding at $> 0.1\%$ intradermal induction concentration OR $\geq 30\%$ responding at $> 1\%$ intradermal induction concentration	$\geq 30\%$ responding at $\leq 0.1\%$ intradermal induction concentration OR $\geq 60\%$ responding at $> 0.1\%$ to $\leq 1\%$ intradermal induction concentration
Beuhler	No positive response or low incidence data	$\geq 60\%$ responding at $> 0.2$ to $\leq 20\%$ topical induction dose OR $\geq 15\%$ responding at $> 20\%$ topical induction dose	$\geq 15\%$ responding at $\leq 0.2\%$ topical induction concentration OR $\geq 60\%$ responding at any topical induction concentration
Qualitative	Negative results	Mixed results	Positive results OR NIOSH SK-SEN notation

4 Worksheet for Skin Sensitization

Skin sensitization (5 points possible)			
Data supports:	Non-sensitizer (Band A)	Moderate sensitizer (Band C)	Extreme sensitizer (Band E)
IF data available, put data, calculations, notes, etc. in this row corresponding to the correct band criteria; otherwise leave blank.			
Source, Rank 1 or 2:			

**DRAFT**

1 *Acute Toxicity*

2 Data Sources

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
Acute Toxicity	1	National Library of Medicine ChemID Plus	ChemID Plus
		U.S. EPA Superfund Chemical Data Matrix	U.S. SCDM
		Pesticide Properties Database	PPDB
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
	2	Hazardous Substance Data Bank	HSDB
		Agency for Toxic Substances & Disease Registry	ATSDR

3 Criteria for Acute Toxicity Endpoint

NIOSH banding criteria for Acute Toxicity					
Exposure/Dosing Route	Band				
	A	B	C	D	E
<b>Oral toxicity (LD<sub>50</sub>)</b>	>2,000 mg/kg-bodyweight	>300 to ≤ 2,000 mg/kg-bodyweight	>50 to ≤ 300 mg/kg-bodyweight	>5 to ≤ 50 mg/kg-bodyweight	≤ 5 mg/kg-bodyweight
<b>Dermal toxicity (LD<sub>50</sub>)</b>	> 2,000 mg/kg-bodyweight	>1,000 to ≤ 2,000 mg/kg-bodyweight	>200 to ≤ 1,000 mg/kg-bodyweight	>50 to ≤ 200 mg/kg-bodyweight	≤ 50 mg/kg-bodyweight
<b>Inhalation gases (LC<sub>50</sub>)</b>	> 20,000 ppmV/4h	>2,500 to ≤ 20,000 ppmV/4h	>500 to ≤ 2,500 ppmV/4h	>100 to ≤ 500 ppmV/4h	≤ 100 ppmV/4h
<b>Inhalation vapors (LC<sub>50</sub>)</b>	> 20.0 mg/liter/4h	>10.0 to ≤ 20.0 mg/liter/4h	>2.0 to ≤ 10.0 mg/liter/4h	>0.5 to ≤ 2.0 mg/liter/4h	≤ 0.5 mg/liter/4h
<b>Inhalation dusts and mists (LC<sub>50</sub>)</b>	> 5.0 mg/liter/4h	>1.0 to ≤ 5.0 mg/liter/4h	>0.5 to ≤ 1.0 mg/liter/4h	>0.05 to ≤ 0.5 mg/liter/4h	≤ 0.05 mg/liter/4h

4 Worksheet for Acute Toxicity

Acute Toxicity (5 points possible)						
Data Supports:		A	B	C	D	E
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.	Oral toxicity (LD <sub>50</sub> )					
	Dermal toxicity (LD <sub>50</sub> )					
	Inhalation gases (LC <sub>50</sub> )					
	Inhalation vapors (LC <sub>50</sub> )					
	Inhalation dusts and mists (LC <sub>50</sub> )					
<b>Source, Rank 1 or 2:</b>						

5 *\*\*If multiple LD50 or LC50 values are found for each route of exposure/chemical state, record only the lowest value in this*  
 6 *chart.*

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**DRAFT**

1 *Skin Corrosion/Irritation*

2 Data Sources

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
<b>Skin Irritation</b>	1	NIOSH Skin Notation Profiles	SK Profiles
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
		Organization for Economic Co-operation and Development	OECD
	2	Agency for Toxic Substances & Disease Registry	ATSDR
		U.S. EPA Integrated Risk Information System	IRIS

3 Criteria for Skin Corrosion/Irritation Endpoint

NIOSH Banding Criteria for <b>Skin Irritation/Skin Corrosion</b>			
<b>Band</b>			
<b>A</b>	<b>B</b>	<b>C</b>	<b>E</b>
Non-irritating	Mild to moderate irritation	Moderate to severe irritation; reversible direct effects OR If results are mixed or indicate irritant potential with severity unspecified	Skin corrosion; irreversible effects  pH value of $\leq 2.0$ or $> 11.5$

4 Worksheet for Skin Corrosion/Irritation Endpoint

<b>Skin irritation/corrosion (5 points possible)</b>				
<b>Data supports:</b>	<b>Non-irritating (Band A)</b>	<b>Mild to moderate irritation; reversible direct effects (Band B)</b>	<b>Moderate to severe irritation; reversible effects OR if results are mixed or indicate irritant potential with severity unspecified (Band C)</b>	<b>Skin Corrosion; irreversible effects OR pH value <math>\leq 2.0</math> or <math>&gt; 11.5</math> (Band E)</b>
<b>If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.</b>				
<b>Source, Rank 1 or 2:</b>				

5

**DRAFT**

1 *Eye Damage/Eye Irritation*

2 Data Sources

ENDPOINT	Rank	SOURCE OF INFORMATION	ACRONYM
<b>Eye Irritation</b>	1	Organization for Economic Cooperation and Development	OECD
		World Health Organization International Programme on Chemical Safety	WHO-IPCS
		European Chemicals Agency; Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH
	2	Agency for Toxic Substances & Disease Registry	ATSDR
		U.S. EPA Integrated Risk Information System	IRIS

3 Criteria for Eye Damage/Eye Irritation Endpoint

NIOSH Banding Criteria for <b>Serious Eye Damage/Eye Irritation</b>			
Band			
A	B	C	E
Non-irritating	Mild to moderate irritation	Severe irritation; moderate to severe irritation OR Irritant with unspecified severity, no conclusion, or mixed results	Irreversible eye damage

4 Worksheet for Eye Damage/Eye Irritation

<b>Eye damage/Eye irritation (5 points possible)</b>				
Data supports:	Non-irritating (A)	Mild to moderate irritation (B)	Severe irritation; moderate to severe irritation; OR no classification system, no conclusion, or mixed results (C)	Irreversible eye damage (E)
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.				
Source, Rank 1 or 2:				

5

**DRAFT**

**1 Section B.5 Full Table for Tier 2 Hazard Banding**

2 If using the electronic version of this spreadsheet, this page will be automatically filled  
3 electronically upon insertion of relevant endpoint specific data. If filling out this table by hand,  
4 each of the preceding endpoint specific tables in section B.4 can be consulted to fill out this full  
5 table. A check mark should be inserted in the appropriate column for each row of data. The  
6 determinant score for each health endpoint/toxicity parameter should be calculated in the  
7 determinant score column. The most protective of all the bands entered is the final Tier 2 OEB  
8 for the chemical.

<b>Chemical Name:</b>			
<b>CAS:</b>			
<b>Endpoint</b>	<b>Data</b>	<b>EDS</b>	<b>Endpoint Band</b>
<b>Acute Toxicity</b>	Source:		
<b>Skin Corrosion/Irritation</b>	Source:		
<b>Serious Eye Damage/ Eye Irritation</b>	Source:		
<b>Respiratory Sensitization</b>	Source:		
<b>Skin Sensitization</b>	Source:		
<b>Genotoxicity</b>	Source:		
<b>Carcinogenicity</b>	Source:		
<b>Reproductive Toxicity</b>	Source:		
<b>Specific Target Organ Toxicity</b>	Source:		
<b>OVERALL Tier 2 BAND</b>		<b>TDS=</b>	

9

# Appendix C: Examples of Chemicals Banded in Tier 1

This appendix provides examples of chemicals that NIOSH has banded by using the Tier 1 process.

## Chemical Name: Bentazone

Chemical Name: Bentazone CAS: 25057-89-0					
Endpoint		Hazard Code	Hazard Category	H-code source	Endpoint Band
Acute Toxicity	Inhalation				C
	Oral	H302	Category 4	GHS	
	Dermal				
Skin Corrosion/Irritation					
Serious Eye Damage/ Eye Irritation		H319	Category 2	GHS	C
Respiratory and Skin Sensitization		H317	Category 1	GHS	C
Germ Cell Mutagenicity					
Carcinogenicity					
Reproductive Toxicity					
Specific Target Organ Toxicity					
Most Protective Band					<b>C</b>

## Result:

Band C is assigned as a result of the Tier 1 evaluation. A Tier 2 evaluation is recommended.

**DRAFT**

1 **Chemical Name: Perfluorooctane Sulfonic Acid**

<b>Chemical Name: Perfluorooctane Sulfonic Acid</b>					
<b>CAS: 1763-23-1</b>					
<b>Endpoint</b>		<b>Hazard Code</b>	<b>Hazard Category</b>	<b>H-code Source</b>	<b>Endpoint Band</b>
<b>Acute Toxicity</b>	<b>Inhalation</b>	H332	Category 4	GHS	<b>C</b>
	<b>Oral</b>	H302	Category 4	GHS	
	<b>Dermal</b>				
<b>Skin Corrosion/Irritation</b>		H314	Category 1B	GHS	<b>E</b>
<b>Eye Damage/Eye Irritation</b>					
<b>Respiratory and Skin Sensitization</b>					
<b>Germ Cell Mutagenicity</b>					
<b>Carcinogenicity</b>		H351	Category 2	GHS	<b>E</b>
<b>Reproductive Toxicity</b>		H360D	Category 1B	GHS	<b>D</b>
<b>Specific Target Organ Toxicity</b>		H372	Category 1	GHS	<b>E</b>
<b>Most Protective Band</b>					<b>E</b>

2 **Result:**

3 **Band E is assigned as a result of the Tier 1 evaluation. A Tier 2 evaluation is optional.**

## Appendix D: Example of Chemical Banded in Tier 2

This appendix provides an example of a chemical NIOSH has banded by using the Tier 2 process.

**Chemical Name: Benzo (k) Fluoranthene**

**CAS Number: 207-08-09**

- Toxicity information for benzo (k) fluoranthene was found for the following endpoints: carcinogenicity, genotoxicity, skin irritation and eye irritation. Determinant scores were assigned as 30, 5, 5, and 5, respectively. No source data were found for reproductive toxicity, respiratory sensitization, skin sensitization, specific target organ toxicity, or acute toxicity. The completed worksheet for the relevant health endpoints follow:

<b>Carcinogenicity (20 or 30 points possible)</b>					
	<b>Band A</b>	<b>Band B</b>	<b>Band C</b>	<b>Band D</b>	<b>Band E</b>
<b>NTP/EPA/IARC/Canada/California (QUALITATIVE)</b>					EPA IRIS B2 - Probable human carcinogen - based on sufficient evidence of carcinogenicity in animals.
<b>EPA IRIS Slope Factor</b>					
<b>EPA IRIS Inhalation Unit Risk</b>					
<b>Health Canada TD05</b>					
<b>Health Canada TC05</b>					
<b>California Slope Factor</b>				1.2 (mg/kg-day) <sup>-1</sup>	
<b>California Inhalation Unit Risk</b>				1.1x10 <sup>-4</sup> (ug/m <sup>3</sup> ) <sup>-1</sup>	

- Cancer data was retrieved from EPA IRIS and CalOEHHA because both qualitative and quantitative data were available, the quantitative data takes precedence for cancer. The endpoint-specific band for cancer is, therefore, **band D** based on the slope factor and inhalation unit risk values. A determinant score of 30 is assigned on the basis of presence of quantitative data.

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<b>Genotoxicity (5 points possible)</b>			
<b>Data supports:</b>	<b>Negative Results (Band A)</b>	<b>Mixed Results (Band C)</b>	<b>Positive Results (Band E)</b>
<b>If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.</b>			Salmonella (023963) Completed : Positive
<b>Source, Rank 1 or 2:</b>			NTP

- 1 • One positive in vivo result was found for genotoxicity. The endpoint-specific band for  
2 genotoxicity is band E, and a determinant score of 5 is assigned.  
3

<b>Skin irritation/corrosion (5 points possible)</b>				
<b>Data supports:</b>	<b>Non-irritating (Band A)</b>	<b>Mild to moderate irritation; reversible direct effects (Band B)</b>	<b>Moderate to severe irritation; reversible effects OR if results are mixed or indicate irritant potential with severity unspecified (Band C)</b>	<b>Skin Corrosion; irreversible effects OR pH value <math>\leq 2.0</math> or <math>&gt; 11.5</math> (Band E)</b>
<b>If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.</b>			Irritation, severity unspecified	
<b>Source, Rank 1 or 2:</b>			ECHA/REACH	

- 4 • In the REACH database, benzo (k) fluoranthene is described as irritating to the skin, but the  
5 severity is not specified. Band C is assigned, and a determinant score of 5 is assigned.

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<b>Eye irritation/corrosion (5 points possible)</b>				
Data supports:	Non-irritating (A)	Mild to moderate irritation (B)	Severe irritation; moderate to severe irritation; OR no classification system, no conclusion, or mixed results (C)	Serious or irreversible eye damage (E)
If data available, put data in this row corresponding to the correct band criteria; otherwise leave blank.			Irritation and photosensitivity described. No indication of severity.	
Source, Rank 1 or 2:			HSDB	

- In the REACH database, benzo (k) fluoranthene is described as causing eye irritation and photosensitivity, but the severity is not specified. Band C is assigned, and a determinant score of 5 is assigned.

**Result:**

**Based on the available data, a TDS of 45 is calculated. This TDS exceeds the threshold for data sufficiency (TDS≥30). The most protective band assigned is band E. The final Tier 2 band for benzo (k) fluoranthene is band E, on the basis of genotoxicity.**

# 1 Appendix E: Chemicals

2 The following is a list of chemicals used for the evaluation exercises described in Chapter 6.

- |  |                                     |   |
|--|-------------------------------------|---|
| 1. Potassium Bromate                     | 35. Anisidine p-                    | 70. Methoxy-2-propanol [PGME] 1-              |
| 2. Mancozeb                              | 36. Butyl acetate sec-              | 71. Nitropropane 1-                           |
| 3. Nitrochlorobenzene p-                 | 37. Caprolactam - Vapor             | 72. Vinyl acetate                             |
| 4. Nitroaniline p-                       | 38. Ethyl butyl ketone              | 73. Methyl isobutyl ketone                    |
| 5. Terephthalic acid                     | 39. Xylene p-                       | 74. Methyl isobutyl carbinol                  |
| 6. Dinitrobenzene p-                     | 40. Cresol p-                       | 75. Diisopropylamine                          |
| 7. Diethylaminoethanol 2-                | 41. Dichlorobenzene p-              | 76. Isopropyl ether                           |
| 8. Vinylcyclohexene                      | 42. Toluidine p-                    | 77. Isopropyl acetate                         |
| 9. Ethyl benzene                         | 43. Phenylenediamine p-             | 78. Acetic anhydride                          |
| 10. Styrene - monomer                    | 44. Quinone                         | 79. Maleic anhydride                          |
| 11. Benzyl chloride                      | 45. Vinyl cyclohexene dioxide       | 80. Xylene m-                                 |
| 12. Benzyl Alcohol                       | 46. 1,2-Epoxybutane                 | 81. Cresol m-                                 |
| 13. Benzaldehyde                         | 47. Epichlorohydrin                 | 82. Toluidine m-                              |
| 14. Methyl aniline N-                    | 48. Glycidyl Methacrylate           | 83. Phenylenediamine m-                       |
| 15. Phenylhydrazine                      | 49. Allyl glycidyl ether            | 84. Resorcinol                                |
| 16. Ethylmorpholine N-                   | 50. Ethylene dibromide              | 85. Propylene Glycol Monomethyl Ether Acetate |
| 17. Nitrous oxide                        | 51. Propargyl Bromide               | 86. Trimethyl benzene [Mesitylene] 1,3,5-     |
| 18. Sulfur monochloride                  | 52. Butane                          | 87. Trichlorobenzene 1,3,5-                   |
| 19. Phosphorus oxychloride               | 53. Butadiene 1,3-                  | 88. Melamine                                  |
| 20. Phosphorus pentachloride             | 54. Allyl chloride                  | 89. Isocyanuric Acid                          |
| 21. Ozone - Heavy work                   | 55. Ethylene dichloride             | 90. Diisobutyl ketone                         |
| 22. Hydrogen bromide                     | 56. Ethylene chlorohydrin           | 91. Hexyl acetate sec-                        |
| 23. Chlorine dioxide                     | 57. Propionitrile                   | 92. Methylcyclohexane                         |
| 24. Methylene bisphenyl isocyanate [MDI] | 58. Acrylonitrile                   | 93. Toluene                                   |
| 25. Methylene dianiline 4,4'-            | 59. Ethylenediamine                 | 94. 4-Picoline                                |
| 26. Phenyl ether - Vapor                 | 60. Allyl alcohol                   | 95. Chlorobenzene                             |
| 27. Nitric oxide                         | 61. Propargyl alcohol               | 96. Cyclohexylamine                           |
| 28. Nitrogen dioxide                     | 62. Ethylene glycol                 | 97. Cyclohexanol                              |
| 29. Dicyclopentadienyl iron              | 63. Glyoxal                         | 98. Cyclohexanone                             |
| 30. Triethanolamine                      | 64. Methyl formate                  | 99. Phenol                                    |
| 31. Dibutylaminoethanol 2-N-             | 65. Hexylene glycol                 | 100. Phenyl mercaptan                         |
| 32. Cobalt carbonyl (as Co)              | 66. TEPP [Tetraethyl pyrophosphate] | 101. 3-Picoline                               |
| 33. Barium chromate (as Cr)              | 67. Dibutyl phosphate               | 102. 2-Picoline                               |
| 34. Ethylhexanol 2-                      | 68. Methyl pentane 2-               |   |
|  | 69. Methyl propyl ketone            |   |

## DRAFT

103. Isopropoxyethanol 2-  
104. Propyl acetate n-  
105. Pentane n-  
106. Butylamine n-  
107. Malononitrile  
108. Butyl mercaptan n-  
109. Methoxyethanol 2-  
110. Methylal  
111. Diethylamine  
112. Ethyl formate  
113. Tetrahydrofuran  
114. Methyl isoamyl ketone  
115. Isobutyl acetate  
116. Methyl n-amyl ketone  
117. Methoxyethyl acetate 2-  
118. Hexane n-  
119. Succinonitrile  
120. Valeraldehyde n-  
121. Ethoxyethanol [EGEE]  
2-  
122. Cyclohexane  
123. Cyclohexene  
124. Pyridine  
125. Piperidine  
126. Morpholine  
127. Chlorodiphenyl (54%  
chloride)  
128. Nickel oxide  
129. Ethoxyethyl acetate  
[EGEEA] 2-  
130. n-Hexyl Alcohol  
131. Glutaraldehyde  
132. Diethylene triamine  
133. Diethanolamine  
134. Dichloroethyl ether  
135. Diethylene Glycol  
136. Octane n-  
137. 1-Octene  
138. Adiponitrile  
139. Butoxyethanol 2-  
140. Nonane - All isomers  
141. 1-Octanol  
142. Diethylene Glycol  
Monoethyl Ether  
143. Methoxyethyl ether  
bis(2-  
144. Zinc potassium chromate  
(as Cr)  
145. Butoxyethyl acetate 2-  
146. Triethylenetetramine  
147. Butoxyethoxy ethanol 2-  
(2-  
148. Tetraethylene Pentamine  
149. Silica, Amorphous --  
Precipitated and gel  
150. Erythromycin  
151. Propoxur  
152. Dimethyl Ether  
153. Endosulfan  
154. Pentaerythritol  
155. Triphenyl phosphate  
156. Fensulfothion  
157. Aldicarb  
158. Tetrafluoroethylene  
159. Decabromodiphenyl  
Oxide  
160. Di(2-  
ethylhexyl)phthalate  
[DEHP]  
161. Dichloro-5,5-dimethyl  
hydantoin 1,3-  
162. Hexachlorobenzene  
[HCB]  
163. Trinitrotoluene [TNT]  
2,4,6-  
164. Butyl chromate (as CrO<sub>3</sub>)  
tert-  
165. Benzophenone  
166. Dimethyl Terephthalate  
167. Catechol  
168. 2,4-Dichlorophenol  
169. Mica  
170. Trichlorobenzene - All  
isomers  
171. Nickel dioxide  
172. Nickel subsulfide (as Ni)  
173. Nickelous hydroxide (as  
Ni)  
174. Tungsten carbide -  
Containing > 2% cobalt,  
as Co  
175. Manganese  
cyclopentadienyl  
tricarbonyl (as Mn)  
176. Dinitrotoluene 2,4-  
177. Vanillin  
178. Triethylamine  
179. Trimethyl phosphite  
180. Dimethylaniline  
181. Malathion  
182. Cyclonite  
183. Isophthalic Acid  
184. Methylcyclopentadienyl  
manganese tricarbonyl 2-  
185. Ammonium chloride -  
Fume  
186. Borates, tetra, sodium  
salts, Pentahydrate  
187. Diphenylamine  
188. Phenyl glycidyl ether  
[PGE]  
189. Phenoxyethanol 2-  
190. Dipropyl ketone  
191. Hydroquinone  
192. Butylated  
hydroxytoluene [BHT] -  
Vapor & Aerosol  
193. Propionaldehyde  
194. Diacetone alcohol  
195. Isoamyl alcohol  
196. Butyraldehyde  
197. Butyl acetate n-  
198. Dioxane 1,4-  
199. Isopentyl acetate  
200. Diallylamine  
201. Adipic acid  
202. 1,6-Hexanediamine  
203. Carbon dioxide  
204. Dimethylamine  
205. Tributyl phosphate

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## DRAFT

- 206.Methylacrylonitrile  
207.beta-Chloroprene  
208.Ferrovandium - dust  
209.Chloro-2-propanol 1-  
210.Tetrachloroethylene  
[Perchloroethylene]  
211.Dimethylacetamide N,N-  
212.Emery  
213.Gallium arsenide  
214.Arsenic pentoxide (as  
As)  
215.Boron oxide  
216.Borates, tetra, sodium  
salts, Decahydrate  
217.Bismuth telluride -  
Undoped  
218.Hexanediol Diacrylate  
219.Calcium hydroxide  
220.Calcium oxide  
221.Terbufos - Vapor &  
aerosol  
222.Iron oxide [Fe<sub>2</sub>O<sub>3</sub>] - dust  
(as Fe)  
223.Magnesium oxide -  
Fume  
224.Antimony trioxide (as  
Sb)  
225.Dimethyl phthalate  
226.Sodium hydroxide  
227.Cyhexatin  
228.Nickel sesquioxide  
229.Zinc oxide - Dust  
230.Phosphorus pentoxide  
231.Tantalum oxide - Dust  
(as Ta)  
232.Vanadium pentoxide -  
Fume (as V<sub>2</sub>O<sub>5</sub>)  
233.Phosphorus pentasulfide  
234.Manganese tetroxide (as  
Mn)  
235.Silica, Crystalline --  
Tripoli  
236.Cresol - mixture of  
isomers  
237.Pentachloronaphthalene  
238.Trichloronaphthalene  
239.Divinyl benzene  
240.Captan  
241.Xylene - Mixed isomers  
242.Borates, tetra, sodium  
salts, Anhydrous  
243.Xylidine - Mixed  
isomers (Vapor &  
aerosol)  
244.Kaolin  
245.Carbon black  
246.Hexachloronaphthalene  
247.Tetrachloronaphthalene  
248.Methyl ethyl ketone  
peroxide [MEKP]  
249.Gypsum  
250.Aluminum oxide  
251.Calcium silicate -  
Synthetic  
252.Nickel carbonyl (as Ni)  
253.Iron pentacarbonyl  
254.Tellurium - Compounds  
(as Te)  
255.Zinc chromate (as Cr)  
256.Sesone  
257.Methyl 2-cyanoacrylate  
258.Thiram  
259.Calcium chromate (as  
Cr)  
260.Butyl lactate n-  
261.d-Limonene  
262.Enflurane  
263.Subtilisins [Proteolytic  
enzymes]  
264.Butylamine sec-  
265.Benzyl acetate  
266.Ethyl acrylate  
267.Butyl acrylate n-  
268.Ethanolamine  
269.Dicrotophos - Vapor &  
Aerosol  
270.Ethyl acetate  
271.Mesityl oxide  
272.Piperazine  
dihydrochloride  
273.Heptane n-  
274.Sodium cyanide (as CN)  
275.Chlordecone  
276.Oxalic acid  
277.Silica, Crystalline --  
Cristobalite  
278.Ferbam  
279.Tri-n-butyltin chloride  
(as TBTO)  
280.m-Xylene alpha,alpha'-  
diamine  
281.Dinitolmide  
282.Sodium  
diethyldithiocarbamate  
283.Talc - Containing no  
asbestos fibers  
284.Silica, Crystalline --  
Quartz  
285.Dimethylethoxysilane  
286.2-Mercaptobenzothiazole  
287.Ethylhexanoic acid -  
Vapor & aerosol 2-  
288.para-Aminobenzoic Acid  
289.Methoxyphenol 4-  
290.Potassium cyanide (as  
CN)  
291.Ethylenimine  
292.Halothane  
293.Silica, Crystalline --  
Tridymite  
294.Dichloroethylene, cis-  
isomer 1-2  
295.Dichloroethylene, trans-  
isomer 1,2-  
296.Calcium cyanamide  
297.TrimethylolpropaneTriac  
rylate  
298.Carbofuran  
299.Methoxy-1-propanol 2-  
300.Butanol (+/-)-2-  
301.Sodium pyridinethione  
302.Methyl tert-butyl ether  
[MTBE]  
303.HFE-7100  
304.HFE-7100

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## DRAFT

- 305.1,3,3,3-Tetrafluoropropylene
- 306.Methomyl
- 307.Triethylene Glycol Diacrylate
- 308.Cobalt hydrocarbonyl (as Co)
- 309.1,1-Dichloro-1-Fluoroethane
- 310.Decaborane
- 311.Benomyl
- 312.Tetraethylene Glycol Diacrylate
- 313.Tin dioxide (as Sn)
- 314.Paraquat dichloride
- 315.Atrazine
- 316.Picloram
- 317.Diborane
- 318.Nitrapyrin
- 319.Pentaborane
- 320.Tributyltin fluoride (as TBTO)
- 321.Benzenesulfonic acid, 5-chloro-2((2-Hydroxy-1-naphthalenyl)-azo)-4-methyl, barium salt (2:1)
- 322.Chlorostyrene o-
- 323.Propoxyethyl acetate 2-
- 324.Paraquat dimethyl sulfate
- 325.Osmium tetroxide
- 326.EPN
- 327.Metribuzin
- 328.Cesium hydroxide
- 329.Tributyltin methacrylate (as TBTO)
- 330.Aluminum hydroxide
- 331.Stannous oxide (as Sn)
- 332.Allyl propyl disulfide
- 333.Chrysene
- 334.Fenamiphos
- 335.Nitrobutyl)morpholine 4-(2-
- 336.Octachloronaphthalene
- 337.Diglycidyl ether [DGE]
- 338.Methyl mercury (as Hg)
- 339.2,3,5,6-Tetrachloropyridine
- 340.Tributyltin linoleate (as TBTO)
- 341.Captafol
- 342.Butyl glycidyl ether [BGE] n-
- 343.Triglycidyl-s-triazinetriene 1,3,5-
- 344.Trimethoxysilane
- 345.Vinyl toluene [Methyl styrene] - Mixed isomers
- 346.Diisobutylene
- 347.Dibutyl phenyl phosphate
- 348.Dinitrotoluene
- 349.Polyethylene Glycols (MW > 200)
- 350.Polypropylene Glycols
- 351.Diethylbenzenes,mixed isomers
- 352.2,4-Toluene Diamine and mixed isomers
- 353.Sulfur hexafluoride
- 354.Methylcyclohexanol
- 355.Terphenyl - Mixed isomers
- 356.Chloro-2-methyl-2,3-dihydroisothiazol-3-one 5-
- 357.Plaster of Paris
- 358.Octyl-4-isothiazolin-3-one 2-
- 359.Sodium azide (as Sodium azide)
- 360.Isooctyl alcohol
- 361.Chlorobenzylidene malononitrile o-
- 362.Sulfuryl fluoride
- 363.Diquat
- 364.Propoxyethanol 2-
- 365.2-Chloro-1,1,1,2-Tetrafluoroethane
- 366.Cyclopentane
- 367.Dehydrolinalool
- 368.Chlorpyrifos
- 369.2-Propenoic Acid, Isooctyl Ester
- 370.Clopidol
- 371.Methyl parathion
- 372.Phorate
- 373.Disulfoton - Vapor & Aerosol
- 374.Ronnel [Fenchlorphos]
- 375.Crufomate
- 376.Naled - Vapor & aerosol
- 377.Hydrazine
- 378.Bis(2-dimethylaminoethyl) ether [DMAEE]
- 379.1,1,1-Trifluoro-2,2-Dichloroethane
- 380.Aldrin
- 381.Chlorinated diphenyl oxide o-
- 382.Bromacil
- 383.Naphthalene diisocyanate [NDI]
- 384.Hexachlorocyclohexane alpha-
- 385.Hexachlorocyclohexane beta-
- 386.Trimethylolpropane Trimethacrylate
- 387.Dibromoneopentyl Glycol
- 388.Diuron
- 389.Diazinon
- 390.Tetramethyl succinonitrile
- 391.Nickelous carbonate
- 392.Diazomethane
- 393.Temephos
- 394.Methoxypropyl) ether [DPGME] bis, (2-
- 395.Pentaerythritol Triacrylate
- 396.Carbonyl fluoride
- 397.1,1,1,2,2-Pentafluoroethane
- 398.Sulprofos
- 399.Lead arsenate (as As)
- 400.Sulfotep [TEDP]

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## DRAFT

401. Zinc yellow (as Cr)  
402. 2-Phosphono-1,2,4 butanetricarboxylic acid  
403. Sodium pyrithione  
404. Ammonium perfluorooctanoate  
405. Sodium Chloroacetate  
406. Zinc beryllium silicate (as Be)  
407. bis-(2-Chloroisopropyl) Ether  
408. Isopropyl glycidyl ether [IGE]  
409. Silicon carbide  
410. Isophorone diisocyanate  
411. Crotonaldehyde  
412. Cyanamide  
413. 1,1,1-Trifluoroethane  
414. Tributyl tin benzoate (as TBTO)  
415. Cyanogen  
416. 1,1,1,3,3-Pentafluoropropane  
417. Ketene  
418. tert-Pentane [Neopentane]  
419. Paraquat  
420. Calcium carbonate  
421. Tetryl  
422. Formaldehyde  
423. DDT [Dichlorodiphenyltrichloroethane]  
424. Benzo[a]pyrene  
425. Acetylsalicylic acid  
426. Aminopyridine 2-  
427. Tetranitromethane  
428. Methylene bis(4-cyclohexylisocyanate)  
429. Trimethyl benzene 1,2,3-  
430. Dinitrobenzene o-  
431. Chloroacetophenone 2-  
432. 3-Methoxypropylamine  
433. Dinitro-o-cresol  
434. Chlorodiphenyl (42% chloride)  
435. Nicotine  
436. Thimerosal  
437. Dichloroethylene, sym-isomer 1-2  
438. Isooctane  
439. Butyl acetate tert-  
440. Ethyl amyl ketone  
441. Dichloropropene 1,3-  
442. Chloromethyl ether bis  
443. Cyclopentadiene  
444. Magnesite  
445. Fenthion  
446. Nitroglycerin [NG]  
447. Trimellitic anhydride  
448. Glycidol  
449. Zinc stearate  
450. Carbon tetrabromide  
451. Carbon tetrachloride  
452. Tri-n-butyltin oxide [TBTO] (as TBTO) bis  
453. Parathion  
454. Chloramphenicol  
455. Glycerin - mist  
456. Ethion  
457. Methyl isopropyl ketone  
458. Urea  
459. Dimethylhydrazine 1,1-  
460. Strychnine  
461. Sucrose  
462. Propylene Glycol  
463. Propiolactone beta-  
464. Chlordane  
465. Sulfur pentafluoride  
466. Lindane  
467. Methylcyclohexanone o-  
468. Toluene-2,4-diisocyanate [2,4-TDI]  
469. Methyl n-butyl ketone  
470. Calcium cyanide (as CN)  
471. Hexene 1-  
472. 1,4-Hexadiene  
473. Vinyl bromide  
474. Methyl acetylene-propadiene mixture [MAPP]  
475. Perchloromethyl mercaptan  
476. Dichloro-1-nitroethane 1,1-  
477. Dimethyl ethylamine N,N-  
478. Chloropropionic acid 2-  
479. Mercaptoethanol  
480. Ethyl ether  
481. Methyl hydrazine  
482. Dieldrin  
483. Chloro-1-nitropropane 1-  
484. Triphenyl amine  
485. Silica, Amorphous -- Fused  
486. Amitrole  
487. Dowtherm Q  
488. Hydrogenated terphenyls - Nonirradiated  
489. Silica, Amorphous - Diatomaceous Earth (uncalcined)  
490. Dinitrotoluene 3,5-  
491. Aniline  
492. Dichlorvos [DDVP] - Vapor & Aerosol  
493. Sodium fluoroacetate  
494. Pentyl acetate 3-  
495. Methylbutyl acetate 2-  
496. Methyl isocyanate  
497. Pentyl acetate tert-  
498. Methoxyacetic acid  
499. Phthalodinitrile m-  
500. Pentyl acetate 2-  
501. Propyl nitrate n-  
502. Pentyl acetate 1-  
503. Hexamethylene Glycol  
504. Carbaryl  
505. Carbon monoxide

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## DRAFT

506. Ethyl tert-butyl ether [ETBE]  
507. Ethanol  
508. Formic acid  
509. Acetic acid  
510. Aminotri (Methylenephosphonic Acid)  
511. Propylene glycol dinitrate  
512. Dioxolane 1,3-  
513. Coal tar pitch volatiles-as benzene-sol. Aerosol  
514. Portland cement  
515. Methanol  
516. Isopropanol [Isopropyl alcohol]  
517. Acetone  
518. Chloroform  
519. Dimethyl Sulfoxide  
520. Hexachloroethane  
521. Thioglycolic acid  
522. Dimethylformamide  
523. Methyl silicate  
524. Diesel fuel - Vapor & aerosol  
525. Hexafluoroacetone  
526. Diesel fuel No. 2 - Vapor & aerosol  
527. Liquified petroleum gas [L.P.G.]  
528. Silica, Amorphous - Diatomaceous earth (calcined)  
529. Dowtherm Q  
530. 1,1,1,3,3,3-Hexafluoropropane  
531. Monocrotophos - Vapor & Aerosol  
532. Heptachlor epoxide  
533. Methoxy-1-propyl acetate 2-  
534. Ethyl cyanoacrylate  
535. Propanol n-  
536. Butanol n-  
537. n-Amyl Alcohol  
538. Benzene  
539. Methyl chloroform  
540. Endrin  
541. Methoxychlor  
542. Methyl bromide  
543. Methyl chloride  
544. Methyl iodide  
545. Methylamine  
546. Hydrogen cyanide (as CN)  
547. Methyl mercaptan  
548. Ethyl bromide  
549. Chlorobromomethane  
550. Propane  
551. Methyl acetylene  
552. Sulfometuron methyl  
553. Aluminum - Metal dust  
554. Lead - elemental and inorganic compounds (as Pb)  
555. Manganese - Elemental & inorganic cmpds (as Mn)  
556. Mercury - Alkyl compounds (as Hg)  
557. Molybdenum - Soluble compounds (as Mo)  
558. Nickel - Soluble inorganic compounds (as Ni)  
559. Platinum - Metal  
560. Rhodium - Soluble compounds (as Rh)  
561. Silicon  
562. Silver - Soluble compounds (as Ag)  
563. Tantalum - Metal  
564. Thallium - Soluble compounds (as Tl)  
565. Tin - Metal  
566. Tin - Organic compounds (as Sn)  
567. Tungsten - Insoluble compounds (as W)  
568. Antimony - Compounds (as Sb)  
569. Arsenic - Elemental  
570. Barium - Soluble compounds (as Ba)  
571. Beryllium - Compounds (as Be)  
572. Cadmium - Metal & compounds (as Cd)  
573. Graphite  
574. Chromium (VI) compounds (as Cr)  
575. Cobalt - Elemental / Metal  
576. Copper - Fume (as Cu)  
577. Hafnium and compounds, as Hf  
578. Uranium (Natural) - Insoluble compounds (as U)  
579. Yttrium - Compounds (as Y)  
580. Zirconium - Compounds (as Zr)  
581. Indium and compounds (as In)  
582. Sulfur dioxide  
583. Lead phosphate (as Pb)  
584. Selenium sulfide (as Se)  
585. Ethyl chloride  
586. Vinyl chloride  
587. Vinyl fluoride  
588. Ethylamine  
589. Acetonitrile  
590. Acetaldehyde  
591. Ethyl mercaptan  
592. Dichloromethane  
593. Difluoromethane  
594. Formamide  
595. Carbon disulfide  
596. Ethylene oxide  
597. Bromoform  
598. Isobutane  
599. 2-Chloropropane  
600. Isopropylamine  
601. Dichloroethane 1,1-  
602. Vinylidene chloride

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## DRAFT

- 603.1,1-Difluoroethane  
604. Vinylidene fluoride  
605. Dichlorodifluoromethane [FC-21]  
606. Phosgene  
607. Chlorodifluoromethane [FC-22]  
608. Iodoform  
609. Trimethylamine  
610. Nitromethane  
611. Propylene imine  
612. Propylene oxide  
613. Difluorodibromomethane  
614. Trifluorobromomethane [F-13B1]  
615. Butanol tert-  
616. 1-Chloro-1, 1-Difluoroethane  
617. Trichlorofluoromethane [FC-11]  
618. Dichlorodifluoromethane [FC-12]  
619. Chlorotrifluoromethane [FC-13]  
620. Tetramethyl lead (as Pb)  
621. Dimethylbutane 2,2-  
622. Acetone Cyanohydrin  
623. 2,2,2-Trifluoroethanol  
624. Dichloropropionic acid 2,2-  
625. 2,3,3,3,- Tetrafluoropropene  
626. Titanium Tetrachloride  
627. Iodine  
628. Lithium hydride  
629. Pentachloroethane  
630. Trichloroacetic acid  
631. Chloropicrin  
632. Tetrachloro-2,2-difluoroethane [FC-11 2a] 1,1,1,2-  
633. Tetrachloro-1,2-difluoroethane [FC-112] 1,1,2,2-  
634. Trichloro-1,2,2-trifluoroethane [FC-113] 1,1,2-  
635. Dichlorotetrafluoroethane [Cryofluorane]  
636. Chloropentafluoroethane  
637. Heptachlor  
638. Perchloryl fluoride  
639. Sodium bisulfite  
640. Dichloro-2-butene 1,4-  
641. Zinc chloride - Fume  
642. Hydrogen chloride  
643. Phosphoric acid  
644. Hydrogen fluoride  
645. Ammonia  
646. Sulfuric acid  
647. Isopropylaniline N-  
648. Sodium metabisulfite  
649. Nitric acid  
650. Hexachlorocyclopentadiene  
651. Dicyclopentadiene  
652. Dimethyl sulfate  
653. Nickel chloride (as Ni)  
654. Phosphorus trichloride  
655. Hydrogen peroxide  
656. Tetrasodium pyrophosphate  
657. Phosphorus (yellow)  
658. Bromine  
659. Barium sulfate  
660. Chromic acid and Chromates (as CrO<sub>3</sub>)  
661. Lead chromate (as Cr)  
662. Diesel fuel No. 4 - Vapor and aerosol  
663. Ammonium sulfamate  
664. Sodium persulfate (as S<sub>2</sub>O<sub>8</sub>)  
665. Calcium sulfate  
666. Arsenous acid, arsenic acid and salts (as As)  
667. Fluorine  
668. Graphite - All forms except graphite fibers  
669. Selenium - Inorganic compounds (as Se)  
670. Chlorine  
671. Germanium tetrahydride  
672. Hydrazoic acid  
673. Hydrogen sulfide  
674. Hydrogen selenide  
675. Oxygen difluoride  
676. Nitrogen trifluoride  
677. Selenium hexafluoride  
678. Tellurium hexafluoride  
679. Lead arsenate (as As)  
680. Mevinphos  
681. Nickel sulfate (as Ni)  
682. Strontium chromate (as Cr)  
683. Bromine pentafluoride  
684. Tetraethyl lead (as Pb)  
685. Ethyl silicate  
686. Triorthocresyl phosphate  
687. Dioxathion - Vapor & Aerosol  
688. Triethylphosphate  
689. Isophorone  
690. Isopentane  
691. Isoprene  
692. Isobutylamine  
693. Isobutyronitrile  
694. Isobutyl alcohol  
695. Isobutyraldehyde  
696. Propylene dichloride  
697. Chloro-1-propanol 2-  
698. Butanol sec-  
699. Methyl ethyl ketone [MEK]  
700. Phosphine  
701. Antimony hydride [Stibine]  
702. Silicon tetrahydride [Silane]  
703. Trichloroethane 1,1,2-

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## DRAFT

704. Trichloroethylene  
705. Chloroacetyl chloride  
706. Acrylamide  
707. Propionic acid  
708. Acrylic acid  
709. Monochloroacetic Acid  
710. Methyl acetate  
711. Nitroethane  
712. Acetylene tetrabromide  
713. Dimethylbutane 2,3-  
714. Tetrachloroethane  
1,1,2,2-  
715. Chlorotrifluoroethylene  
716. Methacrylic acid  
717. Nitropropane 2-  
718. Cumene Hydroperoxide  
719. Oxybis(benzenesulfonyl  
hydrazide) p,p'-  
720. Methyl methacrylate  
721. Chlorinated camphene  
722. Petroleum distillates  
[Naphtha]  
723. Paraffin wax -Fume  
724. Pyrethrum  
725. Diphenyl ether /  
Biphenyl mixture (vapor)  
726. Gasoline  
727. Turpentine  
728. Kerosene  
729. Methyl demeton  
730. Rubber solvent  
(Naphtha)  
731. Asphalt (Bitumen) fume  
732. Demeton - Vapor &  
aerosol  
733. Warfarin  
734. 1,1,1,2-Tetrafluoroethane  
735. Pentachloronitrobenzene  
736. Hexamethylene  
diisocyanate [HDI] 1,6  
737. Pindone  
738. Rotenone (commercial)  
739. Diethyl phthalate  
740. Dibutyl phthalate  
741. Phthalic anhydride  
742. Tributyltin naphthenate  
(as TBTO)  
743. Azinphos-methyl -  
Vapor and Aerosol  
744. ANTU  
745. Trichlorobenzene 1,2,3-  
746. Hexachlorobutadiene  
747. Pentachlorophenol  
748. 1-Decene  
749. N-Methyl-2-Pyrrolidone  
750. Nitrotoluene o-  
751. Picric acid  
752. Butylphenol o-sec-  
753. Anisidine o -  
754. Polyvinyl chloride  
[PVC]  
755. Acrylic acid polymer  
756. Cellulose  
757. Starch  
758. Naphthalene  
759. Quinoline  
760. Demeton-S-methyl -  
Vapor & aerosol  
761. Biphenyl  
762. Phenothiazine  
763. Trichlorophenoxyacetic  
acid] 2,4,5-T [2,4,5-  
764. Perlite  
765. Benzoyl peroxide  
766. Dichlorophenoxyacetic  
acid] 2,4-D [2,4-  
767. Fonofos  
768. Indene  
769. Xylene o-  
770. Cresol o-  
771. Chlorotoluene o-  
772. Dichlorobenzene o-  
773. Toluidine o-  
774. Phenylenediamine o-  
775. Trimethyl benzene 1,2,4-  
776. 2,4-Toluene Diamine and  
mixed isomers  
777. Dibromo-3-  
chloropropane 1,2-  
778. Methyl pentane 3-  
779. Trichloropropane 1,2,3-  
780. Diethyl ketone  
781. Methyl Ethyl Ketoxime  
782. Methyl acrylate  
783. Methyl chloroacetate  
784. Thiobis(6-tert-butyl-m-  
cresol) 4,4'-  
785. Disulfiram  
786. TetrahydrofurfurylAlcohol  
787. Furfuryl alcohol  
788. Furfural  
789. Butyltoluene p-tert-  
790. Butylphenol p-tert-  
791. Butylbenzoic acid 4-tert-  
792. Cumene  
793. alpha-Methyl styrene  
794. Acetophenone  
795. Benzoyl Chloride  
796. Nitrobenzene  
797. Nitrotoluene m-  
798. Dinitrobenzene m-  
799. Hydroxybenzoic Acid  
800. n,n-Dimethyl-para-  
toluidine  
801. Nitrotoluene p-  
802. tert-Amyl methyl ether  
[TAME]  
803. Triethoxysilane  
804. Hydroxypropyl acrylate  
2-

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