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Identifying and Prioritizing Hazardous Chemicals in Construction Metal Structure Coating Systems: A Roadmap for Data-Driven Disease Prevention

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ABSTRACT

Introduction: Occupational exposure as a painter was classified by the International Agency for Research on Cancer (IARC) as a Group 1 carcinogen (carcinogenic to humans) in 1989. Chemical agents responsible for cancers and other illnesses among industrial painters are not well-documented. The goal of this systematic review and synthesis was to document the chemistries of metal structure coating systems, summarize data gaps on occupational exposures and health effects among painters, and identify and prioritize hazardous chemicals to guide future exposure and occupational health studies, and ultimately disease prevention efforts.

Methods: We reviewed coating products approved by the Northeast Protective Coating Committee (NEPCOAT) for use in steel bridges in New England, with a special focus on Part B of these reactive chemical systems, and related literature on exposures and health effects.

Results: From the review of safety datasheets (SDS), we identified 61 unique CAS numbers belonging to different Part B chemical groups of isocyanate- and epoxy-based formulations, including amine hardeners, solvents, nanomaterials, and other additives. The list of identified ingredients contained 14 potent sensitizers, two IARC Group 1 known carcinogens, and 7 IARC Group 2B possible carcinogens. Cancers of the lungs, urinary bladder, liver, kidneys, and gastrointestinal system, allergic contact dermatitis, lung fibrosis, and asthma were some possible disease endpoints. Existing occupational exposure studies focused on solvent exposures, while exposure and biomonitoring studies of amine hardeners and other ingredients of concern in these formulations are lacking.

Conclusions: The list of chemicals of concern identified here, including sensitizers and carcinogens, can serve as a basis for analytical method development and field exposure assessment studies. A national multi-pronged strategy to reduce chemical exposures and health risks among construction painters is warranted, including research on exposure monitoring and reduction efforts, longitudinal epidemiological studies, and product reformulation.

1 | Introduction

Painters are an essential workforce in residential, commercial, and industrial construction. According to U.S. Bureau of Labor statistics, the number of construction painter jobs reached approximately 365,300 all over the United States in 2021 [1]. Employments as a painter is predicted to increase by 5.4% by the end of this decade [2].

Industrial painters are a subgroup of painters directly involved with painting and coating of industrial steel structures such as bridges, exterior and interior surfaces of industrial storage tanks, water pipes, wind turbines, and reactive domes [3]. Painting is often referred to as an activity performed for esthetic purposes, while coating is done to ensure surface protection against environmental conditions such as corrosion, heat, sunlight, as well as abrasion and physical wear and tear [3]. In this paper, the terms "coating" and "painting" have been used interchangeably. The demand for industrial painting jobs will continue to grow in response to the need for repairs of the aging infrastructure and expansion of the wind turbines. More than 45,000 bridges in the United States are in need of repair or replacement, requiring, among other services, industrial coating jobs [4, 5]. The new infrastructure bill approved by the US Senate and the Congress includes a budget of $40B for repairing bridges across the country, increasing the demand for bridge painting jobs [6]. The global demand for industrial painting and employment statistics are not known.

Coating of metal structures typically requires application of three different layers of paint to achieve the specified technical performances standards [7]. The first layer consists of an epoxy-based primer system fortified with an anticorrosion element such as zinc and iron that is applied immediately after the surface undergoes abrasive blasting. The second layer (commonly referred to as mid-coat/intermediate coat) is an epoxy-based resin system applied to achieve mechanical bonding between the primer and top layers. The final layer, also referred to as the top-coat, is based on aliphatic isocyanate formulations that protect the surface from deterioration due to UV, temperature changes, moisture, and physical damage. Each layer is typically a two-part (less frequently a three part) reactive chemical system often referred to as Parts A and B [8]. Workers mix these two parts on site right before the product application following the manufacturers' recommendations to achieve the required technical performance specifications. The mixture is then applied using brushes or rollers or sprayed using air spraying guns. Brushes and rollers are typically used to coat difficult-to-reach surfaces, such as corners, and edges, whereas spray painting is preferred for uniform and efficient coating of large surfaces. Product mixing and coating application leads to considerable workers' inhalation and dermal exposures to chemical ingredients in these coating products, including isocyanates, epoxies, and other components of the mixture [9]. Ingestion exposure is also likely, but poorly documented to date.

Occupational exposure as a painter has been classified by the International Agency for Research on Cancer (IARC) as a Group 1, carcinogenic to humans, based on an increased risk of lung and urinary bladder cancers [10–12]. Recent evidence from an international case–control investigation suggest that construction painters have a higher risk for developing lung cancer (OR 1.31, 95% CI 1.11–1.55) compared to other groups of painters [13]. Aside from cancer, painters are at risks for developing other diseases leading to morbidities and mortalities associated with their jobs, including allergic and irritant contact dermatitis (ACD, ICD), isocyanate- and epoxy-induced asthma, hypersensitivity pneumonitis, other respiratory disorders such as pharyngeal irritation, lung function decline, and restrictive lung disorders, as well as urticaria, neuropathy, and cardiovascular disease [14–16]. However, agents responsible for the increased risk of lung and bladder cancer, contact dermatitis, and some other health effects among construction painters are not well documented [13], creating significant barriers for analytical method development, exposure and biomonitoring studies, targeted quantitative exposure assessment for epidemiology and hazard control, exploring exposure–disease associations, disease surveillance, and intervention studies, including product reformulation.

Limited occupational exposure studies to date have focused on Part A reactive components containing isocyanates or epoxies, for the understandable reason of their known potency to cause respiratory and skin sensitization leading to occupational asthma and ACD at extremely low isocyanate levels [17–21]. Our recent exposure assessment and biomonitoring studies among construction metal structure coating painters provide evidence of high potential inhalation and dermal exposures and body burden to isocyanate and epoxy resins during steel structure painting (bridges, wind turbines, and reactor domes) [9, 22, 23]. These studies, to the best of our knowledge, provide the only quantitative data in the literature related to occupational exposures to Part A components in metal structure coating in construction.

In contrast to isocyanate and epoxy formulations in Part A, which are well understood, little is known about occupational exposures, adverse health effects, and toxicity of Part B formulations of these coating systems. Considering different toxicity profiles and target organs of various chemicals in these mixtures, and the complex and poorly understood interactions of various components, it is important to document chemical composition of Part B mixtures in coating products used by construction painters. Subsequent field exposure and health effects studies will also benefit from identifying and prioritizing hazardous chemicals for exposure assessment and biomonitoring. The main objectives of this work were to: (i) document the chemistry and hazardous ingredients in Part B of reactive systems used in construction metal structure coating in New England, with a special focus on two well-documented diseases—cancer and chemical sensitization leading to ACD and asthma; and (ii) identify major data and knowledge gaps related to occupational exposures, biomonitoring, and other adverse health effects of Part B ingredients to prioritize ingredients/chemical groups for subsequent exposure and health effects studies or product substitution.

2 | Materials and Methods

2.1 | Coating Systems Included in the Study

The metal structure coating systems targeted for this review were identified from two main sources: (1) list of products approved by the Northeast Protective Coating Committee

(NEPCOAT) for use in steel bridges in 2020 and (2) coating products identified as part of our larger ongoing study of reactive chemicals in construction. NEPCOAT is an affiliation of northeast states, Connecticut, Massachusetts, Maine, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont that develops acceptance/testing criteria of protective coating for use on highway bridge steel. Our initial screening of coating products used in other states in the United States revealed similar product names with the NEPCOAT systems. Detailed analysis of products used in other parts of the United States and comparisons with Europe and other countries can provide insightful information about product ingredient variability and will be investigated in future studies.

We encountered 16 products at the study sites and identified a total of 25 products in the NEPCOAT system. Since all products identified at the field study sites used for coating of metal structures (e.g., bridges, wind turbines, reactor domes, and elevated water tanks) were also part of the NEPCOAT list, with one exception, the rest of the paper will reference only the NEPCOAT products.

2.2 | Chemical Composition of Coating Products

For each product identified from the NEPCOAT list we performed a detailed review of their safety data sheets (SDS) that were obtained from the manufacturer's websites and Google searches. For each chemical listed in the SDS, we recorded their chemical abstracts service number (CAS number) and reported concentration in the bulk product. Examples of ingredients reported in product SDS are provided in Supporting Information S1: Table S1. First, we developed a full list of all chemicals identified in Part B, stratified by the coating layer (primer, midcoat, and top-coat) and then determined the frequency of occurrence of each unique CAS# across all products. Next, CAS# entries/chemical ingredients were clustered into major groups based on their functionality, consisting of amine hardeners, solvents, nanofillers, and other additives.

For ingredients with limited exposure information (see Section 3.2), we researched and compiled important physicochemical properties that influence exposure pathways, such as the boiling point, vapor pressure, octanol–water partitioning coefficients (log $K_{o/w}$), acidity constants (p*K*a), utilizing data from the National Library of Medicine PubChem database [24], the National Institute for Occupational Safety and Health (NIOSH) pocket guide to chemical hazards [25]. and other handbooks of physical properties of chemicals.

2.3 | Systematic Literature Review on Exposure and Health Effects of Part B Chemicals in Coating Systems

A systematic review of the literature in English was conducted in PubMed and Google Scholar to gather information related to occupational exposures, health effects, and epidemiologic evidence for chemicals identified in Part B formulations (Figure 1). Specific keywords used to extract relevant articles included "amine hardeners," "solvents," "nano," "occupational exposure," "construction painters," "coating systems," and "health effects" and combination thereof. An initial screening of English-only records was done based on their relevance and duplicate records were removed. Articles were excluded from the full-text review if their focus was on automobile and dockyard paints, glues, and dyes, if they were in a language other than English, and if they could not be verified as peer-reviewed or originating from authoritative sources. In addition, the reference lists from the selected full-text articles were reviewed and utilized to identify any additional relevant articles that we might have missed from the searches. The information was updated to include the most recent publications as of the time of this writing. Furthermore, we searched the NIOSH pocket guide for any Recommended Exposure Limits (REL), skin notation designations for chemicals in our list, the OSHA Permissible Exposure Limits (PEL), and the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) [26].

We researched relevant human epidemiological studies, medical case reports, and controlled studies that reported on individual components or a chemical group. Information on cancer and sensitization potential for all chemicals in these mixtures were collected from PubChem [24], Information Network of Departments of Dermatology in Germany (IVDK) [27], Globally Harmonized System (GHS) [28], and the European Chemical Agency (ECHA) [29] databases. A final list of priority chemicals was developed based on the carcinogenicity and allergic sensitization potential, or other adverse health effects.

3 | Results

3.1 | Part B Composition of Products Used in Construction Metal Structure Coating

The review of the NEPCOAT products revealed four product lists, acknowledged as lists A, B, C, and D (Figure 2). The lists differed from each other based on the primer type (organic or inorganic zinc-rich primer) and the number of coats applied over metal surfaces (two or three layers) (Supporting Information S1: Figure S1). The total number of coating systems in all four lists consisted of nine primers, seven intermediate coats, and nine top-coats from four manufacturers.

Primers are three-component systems typically labeled as Part A, B, and F. Part A is based on epoxy resins dissolved in solvents such as methyl ethyl ketone and xylenes, while Part B contains amine hardeners, nanofillers, and other specialty additives dissolved in a blend of solvents, while Part F consists of a corrosion inhibitor such as inorganic zinc powder. Inorganic zinc primers contain zinc metal powder mixed into an inorganic silicate paint binder that can be either a solvent borne (ethyl silicate) or waterborne (alkali silicate). Organic zinc primers contain zinc metal pigment mixed into an organic paint resin such as epoxy or urethane. We identified 42 unique chemicals in Part B across all primers in the NEPCOAT lists consisting of amine hardeners, solvents, nanofillers, and other additives (Supporting Information S1: Table S2).

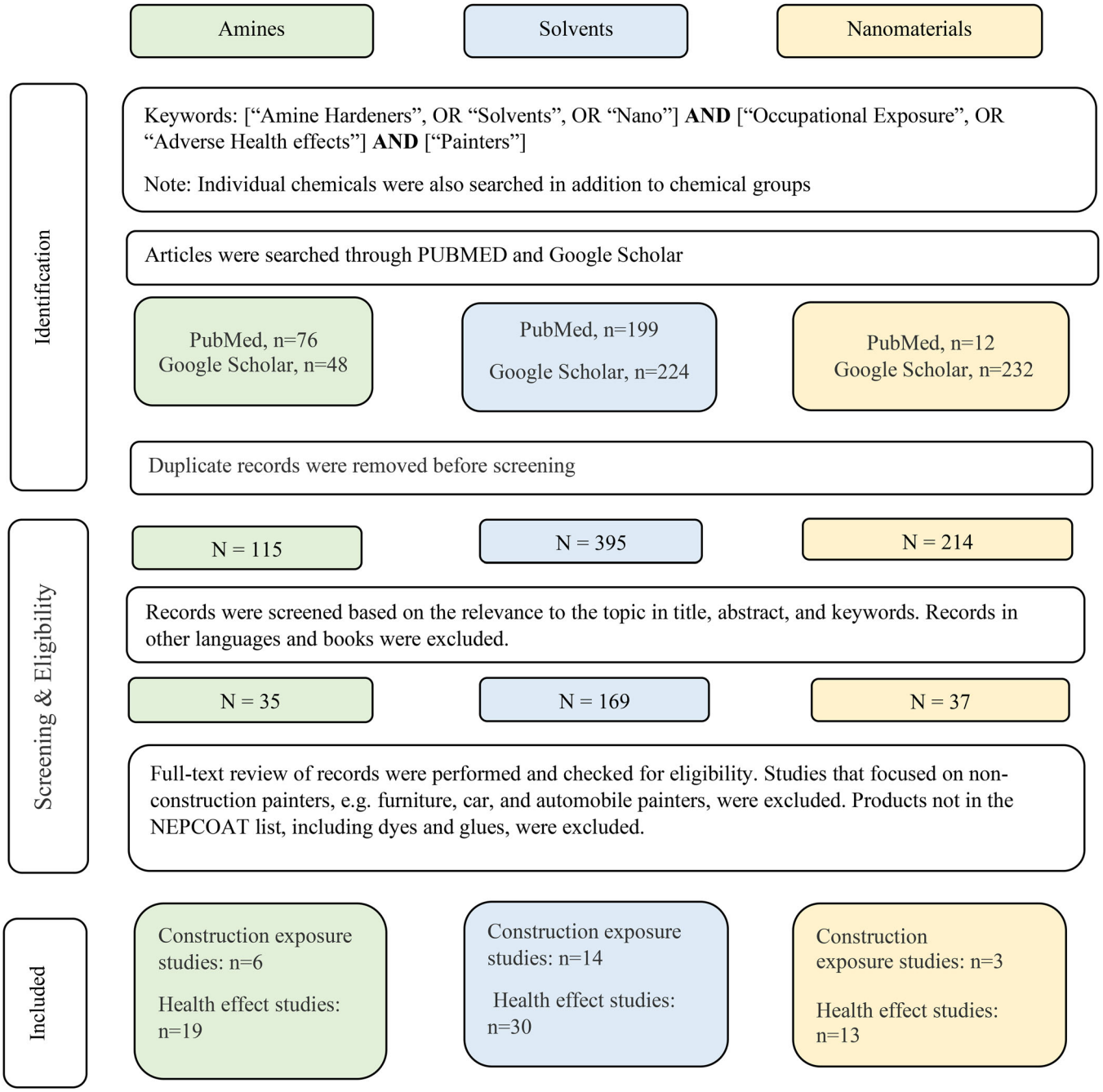

FIGURE 1 | Schematic diagram of the literature review on exposure and adverse health effects of chemicals present in the steel structure coating systems qualified by the Northeast Protective Coating Committee (NEPCOAT).

Intermediate coats are epoxy-based two-component systems. Part A of these systems contain epoxy resins based on bisphenol A diglycidyl ether (BADGE) and its higher oligomers, which can enter polymerization reactions with various cross-linking agents (e.g. amine hardeners, phenols, thiols, acid anhydrides) leading to resin curing [30]. Our review of their SDSs documented 32 distinct chemicals (CAS#) in Part B across all intermediate coats consisting of amine hardeners, solvents, nanofillers and other additives. One compound was reported as a trade secret (Supporting Information S1: Table S2). Several of these CAS# represent mixtures in themselves. For example, poly (propylene glycol) bis(2-aminopropyl ether) (CAS# 9046-10-0) has at least five distinct compounds. Similarly, polyamidoamide (CAS# 68082-29-1) has several compounds, likely pushing the total number of compounds in intermediate coatings to higher numbers.

Top-coat products were identified in all NEPCOAT lists. They are two-part systems; Part A is based on prepolymers of 1,6-hexamethylene diisocyanate (1,6-HDI) or isophorone diisocyanate (IPDI). New Part A chemistries based on acrylic polyurethanes and polysiloxanes are also recommended although we have not encountered them in any of the visited sites. Part B of these top-coats includes polyols (cross-linking agent for isocyanates) dissolved in solvent

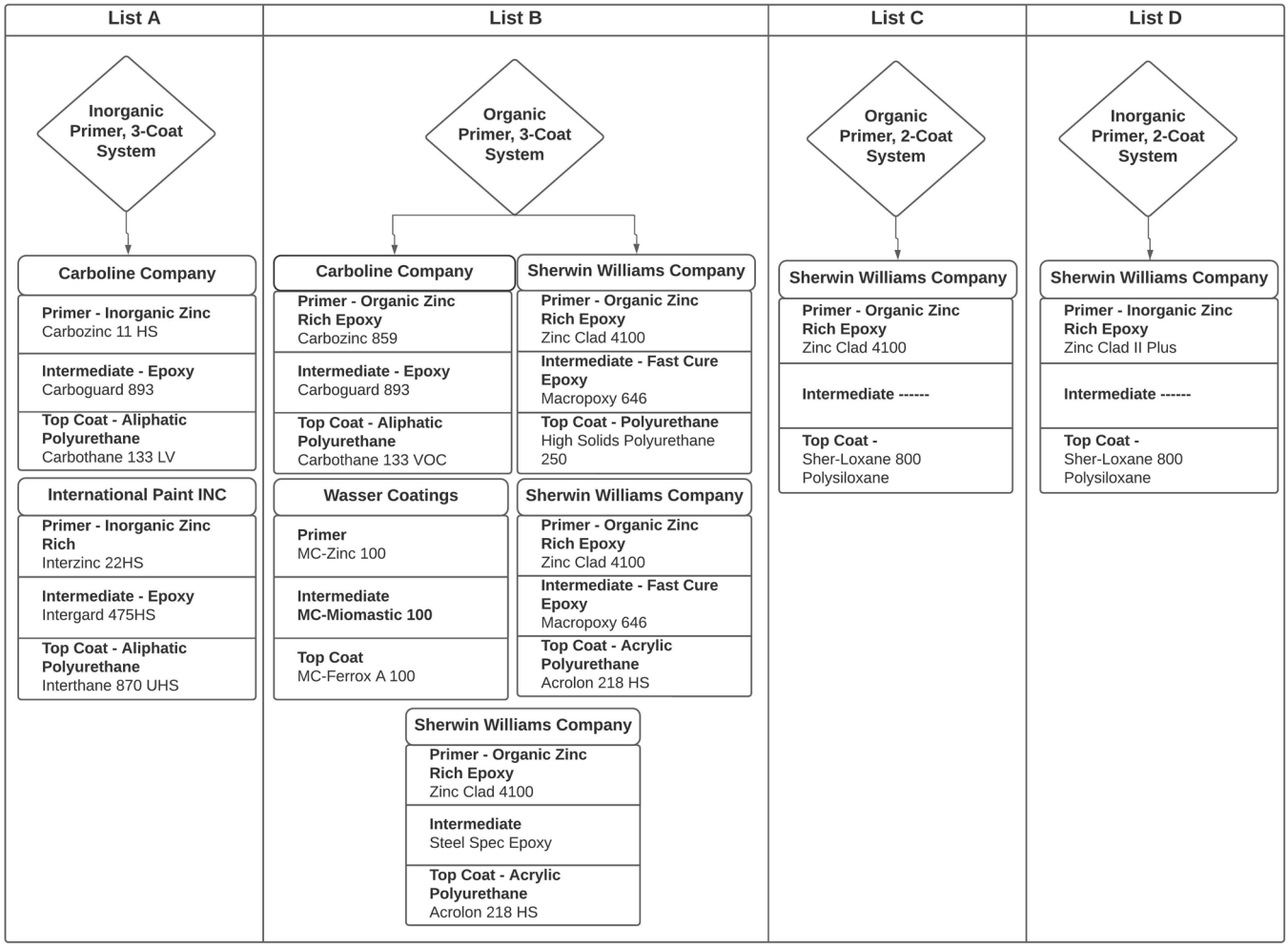

FIGURE 2 | Coating systems approved by the Northeast Protective Coating Committee (NEPCOAT) for use in steel structures.

blends and other additives. We identified 26 unique (CAS #) chemicals in Part B of the top-coat products (Supporting Information S1: Table S2). One compound was reported as a trade secret. Examples include solvent blends (e.g. methyl ethyl ketone, toluene, ethylbenzene, xylenes, 1,3,5-trimethylbenzene, 2-butoxyethanol), polyols, amine hardeners, and nano- or micron-size particulate additives such as titanium dioxide, zinc, iron oxides, and respirable crystalline silica.

3.1.1 | One Component Coating System

We identified two one-part coating systems that did not require pre-mixing of the two separate components. These are pre-mixed products that contain isocyanates, fillers, and solvents. Once the mixture comes into contact with the air moisture, a chain of chemical reactions is initiated, leading to polymerization reactions and the product hardens. One of these products, a Corothane I-MIO-Zinc moisture cure urethane, was used at one of the study sites, while the other was listed in list B of NEPCOAT products. These are complex mixtures similar to the 2- and 3-part systems; however, they do not contain epoxy or amine hardeners (Supporting Information S1: Table S3). For example, Corothane I-MIO-Zinc contains 4,4'-methylene diphenyl diisocyanate (4,4'-MDI), polymeric MDI, the moisture scavenger *p*-toluene sulfonyl isocyanate, iron oxide, chromium oxide, and crystalline silica and was mixed with zinc dust before its application. The Corothane I-Ironox-B moisture cure urethane contains polymeric MDI, toluene diisocyanate prepolymer, as well as the moisture scavenger *p*-toluene sulfonyl isocyanate, iron oxide, and crystalline silica (Supporting Information S1: Table S3) among others.

3.2 | Part B Chemical Ingredients Reported in the SDS of Products

A detailed list of all ingredients identified from product SDS is provided in Table 1. Based on their intended purpose and chemical functionality, they were grouped into four major chemical groups: (1) amine hardeners, containing 12 distinct CAS#; (2) solvents, containing 28 entries as distinct CAS#; (3) nanomaterials and particulate additives, including 19 unique CAS#; and (4) other additives that are chemicals that did not belong in groups 1–3. Overall, three chemicals listed in the SDS were reported as trade secret (Table 1). They included an amine hardener and two specialty additives, one each in mid-coat and top-coat. These major groups are discussed in detail in subsequent sections in the context of occupational exposures and health effects.

TABLE 1 | Chemical ingredients in Part B of NEPCOAT approved two- or three-component coating systems listed by products' safety data sheets (SDS).

Nr.	Chemical name	Abbreviations	Freq[a]	CAS number	% (w/w)	Layer[b]
Amine hardeners[c]						
1	Bis (1,2,2,6,6-pentamethyl-4-piperidyl) sebacate	bPMPS	5	41556-26-7	≤ 5	T
2	Polyamido amine	PAMAM	4	68082-29-1	10–25	P, M
3	2,4,6-Tris dimethyl aminomethyl phenol	Tris-DMP	4	90-72-2	1.0–10	P, M
4	Pentamethyl piperidyl sebacate/methyl 1,2,2,6,6-pentamethyl-4-piperidyl sebacate	PMPS	4	82919-37-7	≤ 1	T
5	1,2-Diamino cyclohexane	DACH	3	694-83-7	1.0–10	P, M
6	Polyoxypropylenediamine/Poly (propylene glycol) bis(2-aminopropyl ether)	POPD/ Jeffamine-D400	3	9046-10-0	2.5–10	P, M
7	Triethylene tetramine	TETA	3	112-24-3	0.3–0.64	P, M
8	Triethoxysilyl propyl amine	TESPA	2	919-30-2	50–90	T
9	Cycloaliphatic amine	CAM	2	*Trade Secret*	1.0–2.5	M
10	Fatty acid amine	FAA	2	85711-55-3	≤ 0.3	P, M
11	3-Aminopropyl trimethoxy silane	APTMS	1	13822-56-5	10–25	T
12	Polyamide	PAmD	1	68410-23-1	10.01	M
Solvents						
1	Methyl *N*-amyl ketone	MAK	21	110-43-0	1–75	P, M, T
	Methyl ethyl ketone,	MEK		78-93-3		
	Methyl isobutyl ketone	MIK		108-10-1		
2	Ethyl benzene/benzyl alcohol		19	100-41-4 100-51-6	0.1–1.0	P, M, T
3	Xylene/mixed isomers		17	1330-20-7 108-38-3 106-42-3	1.0–34	P, M, T
4	Light aromatic hydrocarbons Medium aromatic hydrocarbons Petroleum naphtha Naphthalene		15	64742-95-6 100-51-6 64742-94-5 91-20-3	1–25	P, M, T
5	Toluene		13	108-88-3	0.3–50	P, M, T
6	Heavy/medium aliphatic solvent		10	64742-82-1 64742-88-7 64742-94-5 64742-47-8	≤ 0.3	M, T
7	1,3,5-Trimethylbenzene	TMB	9	108-67-8	1.0 − 10	P, T
	1,2,4-Trimethylbenzene			95-63-6		
	1,2,3-Trimethylbenzene			526-73-8		
8	*N*-butyl acetate, *t*-butyl acetate		8	123-86-4 540-88-5	1.0–10	P, M, T
9	Isopropanol		5	67-63-0	1.0–25	P, M
10	Ethanol		4	64-17-5	10–50	P
11	1-Methoxy-2-propyl acetate	PGMEA	4	108-65-6	1.0–5	P, M, T
12	1,2-Benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters	BDC	4	68515-43-5	1–10	M
13	4-Chlorobenzotrifluoride/*p*-chloro-α,α,α-trifluorotoluene	PCBTF	3	98-56-6	1.0–25	P, M, T

(Continues)

TABLE 1 | (Continued)

Nr.	Chemical name	Abbreviations	Freq[a]	CAS number	% (w/w)	Layer[b]
14	Phenol, isobutylenated methylstyrenated		3	68457-74-9	10–25	M, T
15	4-Morpholinecarboxaldehyde		3	4394-85-8	< 5	T
16	Dipropylene glycol methyl ether/(2-methoxymethylethoxy) propanol	DPGME	3	34590-94-8	1.0–10	P
17	2-Butoxyethanol		2	111-76-2	1.0–10	P, M, T
18	1-Methyl-2-pyrrolidone	NMP	2	872-50-4	0.10–1.0	P
19	Polycarboxylic acid ester/Fatty acids, C14-18 and C16-18-unsatd., 2-phenoxyethyl esters, maleated		2	91001-64-8	< 1	P
20	Dimethyl carbonate		1	616-38-6	2.5–10	T
21	Propylene glycol monomethyl ether	PGME	1	107-98-2	2.5–10	P
22	Methanol		1	67-56-1	≤ 9.1	P
23	Cumene		1	98-82-8	< 1	P
24	Trimethyl borate		1	121-43-7	10–21	P
25	Dibutyltin bis(2,4-pentadionate)/Dibutyltin bis(acetylacetonate)		1	22673-19-4	≤ 10	P
26	Dibutyltin dilaurate		1	77-58-7	≤ 10	T
27	Ethyl 3-ethoxypropionate		1	763-69-9	1.0–10	T
28	2,4-Pentanedione		1	123-54-6	0.1–1.0	T
Nanomaterials						
1	Crystalline silica, respirable or non-respirable powder/quartz/microcrystalline silica	SiO_2-c	22	14808-60-7	0.1–92	P, M, T
2	Titanium dioxide (anatase/rutile)	TiO_2	16	13463-67-7 1317-80-2	1.0−29.3	P, M, T
3	Amorphous silica/silica gel	SiO_2-a	9	7631-86-9	1.0–10	T
4	Carbon black		6	1333-86-4	0.1−10	M, T
5	Wollastonite	$CaSiO_3$	5	13983-17-0	3−25	T
6	Zinc (dust or fume)	Zn	4	7440-66-6	75−100	P, M
7	Mica		4	12001-26-2	2.5−25	P
8	Limestone (nanofiller)	CaCO3	3	1317-65-3	10.0−75	P
9	Iron oxide	Fe_2O_3	3	1309-37-1	1.0−50	M
10	Ethyl polysilicate/polydiethoxysiloxane		3	11099-06-2	1.0−25	P
11	Ethyl silicate		1	78-10-4	10−25	P
12	Alkyl silicate		1	EPA ACC# 102079	25–50	P
13	Zinc oxide	ZnO	3	1314-13-2	1.0–10	P, M
14	Zeolite (aluminosilicate)		3	1318-02-1	3−10	M
15	Talc (hydrated magnesium silicate)	$3MgO{\cdot}4Si\ O_2{\cdot}H_2O$	3	14807-96-6	1.0–10	M
16	Kaolin (aluminum silicate dihydrate)	$Al_2O_3{\cdot}2SiO_2{\cdot}2H_2O$	2	1332-58-7	1.0–10	P
17	Aluminum silicate	$Al_2O_3{\cdot}SiO_2$	2	66402-68-4	1.0–10	P
18	Chromo antimony compound/chrome antimony titanium buff rutile (known as pigment brown 24)	PBR24 (Ti, Cr, Sb)O_2	2	68186-90-3	< 5	T
19	Barium sulfate	$BaSO_4$	2	7727-43-7	10−25	M

(Continues)

TABLE 1 | (Continued)

Nr.	Chemical name	Abbreviations	Freq[a]	CAS number	% (w/w)	Layer[b]
Other additives						
1	Polystyrene		2	9003-53-6	2.5−10	M
2	Trade secret		2	—	—	M, T

Note: The epoxy- or isocyanate-based Part A composition was excluded from this table as their chemistries are well-understood, and the primary focus of this review was Part B. Compound CAS number, concentration in products, and intended application (layer) are also listed.
[a]Frequency of appearance of the chemical in the list of ingredients reported from the SDS of products investigated across all recommended products.
[b]Coating layer: M, mid-coat; P, primer; T, top-coat.
[c]Isophorone diamine (IPDA, CAS# 2855-13-2), 4,4′-methylenedianiline (MDA, CAS# 101-77-9), and *meta*-xylylene diamine (*m*-XDA, CAS# 1477-55-0) were not reported in our reviewed NEPCOAT products. These amines appear often in other epoxy-based construction products, such as glues, and should be kept in mind when investigating amine hardeners in epoxy-based coatings.

3.3 | Occupational Exposures to Part B Chemicals in Metal Coating Systems

3.3.1 | Amine Hardeners

Amine hardeners are used in these products to cross-link with the epoxide and form the polymeric network that provides mechanical strength, chemical resistance and insulation. Most of the amine hardeners identified were present in primers and mid-coat products, while only four of them were found in top-coats. Both aliphatic (primary, secondary, tertiary) and aromatic amines were identified. While aliphatic amines can react with epoxy resins at room temperature, aromatic amines require high temperature for curing [31]. The most frequently used amine was bis (1,2,2,6,6-pentamethyl-4-piperidyl) sebacate (bPMPS) and the highest concentrations in the bulk product were reported for triethoxysilyl propylamine (TESPA) at 50%–90% by weight, both found in top-coat products (Table 1).

Quantitative exposure studies that document occupational exposures to amine hardeners in coating products used in construction jobs are limited. Almost all existing occupational studies are controlled human studies (patch testing or skin prick testing) to identify specific amine hardeners responsible for ACD or skin sensitization among industrial painters using resin systems and assessing their potency. These studies were mostly conducted in Scandinavian countries in Europe from 1991 to 2019 (Supporting Information S1: Table S4), with the Finnish group leading the way. A Norwegian study of industrial painters identified allergens from a list of nine epoxy compounds and amine hardeners using questionnaires and patch tests and focused on a number of chemicals in epoxy resin systems among industrial painters [32]. Aalto-Korte et al. in 2014 and 2015 reported Tris-DMP exposure as the potential cause for occupational contact allergy cases among construction worker painters in Finland [33, 34]. A study of construction workers (including bricklayers and tilers) in Switzerland utilized patient information from the Information Network of Departments of Dermatology and patch testing and identified 30 allergens that include three amine hardeners (isophorone diamine, *N*-isopropyl-*N*′-phenyl-*p*-phenylenediamine and 2,2,4- or 2,4,4-trimethylhexane-1,6-diamine) [35].

Numerous studies in Finland examined occupational asthma from epoxy-based compounds and amine hardeners like polyamines used in industrial and construction coatings, adhesives, plastic composites, and modern sewage pipe relining materials. In inhalation challenge testing, amine hardeners like *m*-xylenediamine (*m*-XDA), isophorone diamine (IPDA), and TETA were not detected in the air. Ethylenediamine was measured at 0.21 mg/m^3 although it was not identified in the SDS of our products. Even with low levels of amine hardeners in the air, the study provides evidence on the role of systemic sensitization through skin contact in occupational asthma from epoxy resins [36]. Furthermore, several case studies have reported positive patch testing results of skin sensitization to 1,2-diaminocyclohexane (DACH) among laboratory technicians and spray painters exposed to DACH [37]. No exposure studies were identified for two sebacates that are salts or esters of sebacic acid added to the products to improve coating durability.

Exposure field studies of amine hardeners among the US industrial painters are lacking and our years of field experience indicate that awareness among industrial painters and researchers is low. There are no occupational standards for amine hardeners. The majority of amine hardeners identified in NEPCOAT products are semi-volatile compounds with boiling points in the range of 156 (tri (dimethylaminomethyl) phenol [Tris-DMP]) to 267°C (triethelyenetetramine [TETA]) and low vapor pressure under normal conditions (Supporting Information S1: Table S5), suggesting that inhalation of amines will be primarily due to aerosolized particles and much less to vapors (except maybe when high steel temperature is encountered in the summer). Skin exposure is expected from settled aerosol droplets or from direct contact with the neat paint and contaminated tools and surfaces. Most of these amine hardeners are highly water soluble (small Log($K_{o/w}$) −4 to 0); however, PAMAM used in primers and mid-coat (Supporting Information S1: Table S5) has a Log($K_{o/w}$) of 10.3, indicating possible skin penetration. Ingestion is a likely exposure source based on our field observations, but this exposure pathway is the least studied.

3.3.2 | Solvents

Solvents are added to coating products as thinners to dissolve other compounds like pigments, additives, and to adjust paint viscosity [11, 38]. The choice of solvent depends on properties such as polarity, hydrogen-bridge linkages, volatility, surface tension, viscosity, flash point, and flammability, often leading to the need to use solvent blends. In NEPCOAT products, methyl n-amyl ketone (MAK), ethyl benzene, xylene, various fractions

of petroleum distillates, and toluene were encountered frequently (Table 1). The highest concentrations in bulk product correspond to MAK (up to 75%), ethanol (up to 50%), toluene (up to 50%), and xylene (up to 34%).

The solvent 4-chlorobenzotrifluoride was identified in top-coat products from Lists A and B at bulk concentrations up to 25% by weight. This is a volatile organic compound with a boiling point of 139.3°C and high potential for inhalation exposure to its vapors. Its low molecular weight (MW = 180.5) and high lipophilicity (Log K_{ow} = 3.6 at 25°C) suggest potential dermal exposure, although skin permeation predictions solely based on molecular weight and octanol/water partition coefficient are still debatable [39]. IARC documents that exposure to 4-chlorobenzotrifluoride in humans can occur via inhalation, ingestion, and dermal absorption [40]. Occupational exposures to 4-chlorobenzotrifluoride have been measured at paint manufacturing sites at 0.7 ppm [41]. There are no exposure or biomonitoring data to 4-chlorobenzotrifluoride among construction painters.

Occupational exposures to common volatile solvents and total volatile organic compound (TVOC) in coating and painting (Supporting Information S1: Table S6**)** have been investigated since the early 1980s and include xylene, toluene, naphtha, ethylbenzene, and glycols in solvent-based paints applied via roller brush, and spray painting [10, 42–45]. Quain et al. measured exposure to organic solvents during bridge painting and identified important exposure determinants such as paint application methods (spraying, rolling, and brushing), paint coating type (primer, intermediate, and finish coatings), and meteorological conditions (temperature, humidity, and wind speed). Higher air concentrations of TVOC, esters, and ketones, as expected, were reported during spraying compared to rolling and brushing. The highest TVOC exposures were measured during primer and mid-coat application and esters were the highest in top-coat [38]. Park et al. evaluated a more comprehensive list of solvents (e.g., toluene, xylene, methyl ethyl ketone, MIBK, benzene, ethyl benzene, styrene, trichloroethylene, perchloroethylene, n-butyl acetate, iso-butyl acetate, sec-butyl acetate, and *tert*-butyl acetate) during application of epoxy primer and mid-coat in underground parking, indoor office buildings, and outdoor steel structures using oil-based or water-based paints. Outdoor painting with oil-based paint had higher exposures compared to indoor painting [46]. A study by Wang et al. developed a solvent exposure index for construction painters, which accounted for painting activities, use of protection equipment, as well as current and historical distribution of solvent air concentration of various sectors of the construction industry [47].

Exposure to solvents has also been assessed qualitatively using self-reported exposure information [48–51]. Long-term exposure to solvents used in epoxy- and urethane paints by 1000 Finnish male construction painters was measured only based on self-reported exposure history in a cross-sectional questionnaire survey [49, 51]. Also, Jang et al. [48] and Lee et al. [50]. assessed self-reported exposure history in shipyard painters. We did not find any study on biomonitoring of solvent exposures among construction painters.

3.3.3 | Nanomaterials and Other Particulate Additives

A wide range of particulate additives are added to paints and coating formulations as fillers, pigments, corrosion inhibitors, or to enhance the electrical, chemical, mechanical, and physical properties of the final product. These particulate additives have a broad range of particle sizes, from nanoparticles (< 100 nm in primary size) to microparticles, depending on the product type. They can be engineered nanoparticles or nanoparticles derived from natural minerals. The Electronic Library of Construction Occupational Safety and Health (ELCOSH) nano database of engineered nanomaterials (ENM) used in construction lists numerous products containing ENM, including floor paints, spray paints and coatings, grouts, and cement. Some notable entries include manufactured nanoscale crystalline silica, aluminum oxide, cerium oxide, zinc oxide, titanium dioxide (TiO_2), and nanosilver, many of which were encountered in the NEPCOAT products (Table 1). Metal oxides are the most common class of additives. Several reports also list the use of organometallic complexes and metal salts in epoxy resin systems for metal coatings (manganese, Mn^{4+}; nickel, Ni^{2+}; zinc, Zn^{2+}; iron, Fe^{3+}; copper, Cu^{2+}; cobalt, Co^{2+}) and pure metals (aluminum, silver, zinc) [52]. They can account from a few percent (multiple additives) to 100% by weight (Zn powder). Several additives are proprietary, so independent confirmation of their presence in Part B is needed through bulk chemical analysis.

The most frequently used particulate materials in NEPCOAT products were crystalline silica and titanium dioxide. The highest concentration in the bulk was reported for zinc (dust or fume) up to 100% as it was predominantly contained in Part F of the primers; crystalline silica up to 92%, and limestone up to 75% (Table 1). Nanoscale crystalline silica, a small fraction of which is present in the respirable quartz, is of particular interest from a respiratory toxicology standpoint, considering its higher toxicity potency compared to microscopic quartz and the ability to translocate to extrapulmonary organs. This review could not identify with certainty the presence and concentration of nanoscale crystalline silica in coating products. Independent material characterization is needed to ascertain the size and distribution of crystalline silicas in coatings and paints.

Only three studies on exposures to nanomaterials in construction coatings were identified. Two focused on nano titanium dioxide (TiO_2) and one on zinc oxide (Supporting Information S1: Table S7). TiO_2 is a high-volume nanoparticle that has been used widely in construction as white pigment and filler in paints, plastics, and coatings. Many industrial applications use TiO_2 nanopowders, mostly as anatase or anatase/rutile mixtures, with primary particle size diameters of around 20–30 nm. Inhalation of aerosol droplet containing nanoparticle additives and ingestion are the primary exposure routes, since skin penetration is negligible [53]. In a 2011 intelligence bulletin #63, NIOSH recommended a REL of 2.4 mg/m^3 for fine TiO_2 and 0.3 mg/m^3 for ultrafine (including engineered nanoscale) TiO_2. West et al. reported task-based exposure measurements during an airless spray application of the nano-based paints in a chamber study that reproduced relevant indoor spray paint environments [54]. The mean exposure levels for respirable TiO_2 were 0.7 mg/m^3, lower than NIOSH REL for fine TiO_2 but

higher than the REL for ultrafine TiO_2. There are no field studies of TiO_2 exposures among painters.

Zinc dust and zinc oxide (ZnO) were reported in high amounts (% by weight) in primers and mid-coat products of our study. Cooper et al. reported inhalation exposure to zinc and ZnO aerosol during spray application of wood sealants in construction [55]. Mass concentration of respirable zinc measured in the generated aerosol was lower than NIOSH REL for total zinc (5 mg/m^3 time-weighted average) and the maximum concentration measured was 3 mg/m^3. Occupational exposure limits for nanoscale ZnO have not been established [56]. Although the product in the Cooper et al. study is different from the coating products used in industrial coatings, the spray application method is similar, suggesting potentially high nano- and microparticulate exposure during spray painting in industrial coatings that warrants quantitative assessments.

Painters' exposure to other nanomaterials such as antimony- and chromium-containing pigments, respirable and nanoscale crystalline silica used extensively in coating products have not been investigated and quantitative field exposure studies are lacking.

3.4 | Health Effects of Exposures to Part B Chemicals in Metal Coating Systems

The focus of this analysis is to identify and prioritize ingredients in these formulations that are responsible for major adverse health effects. We group these adverse effects into three broad classes— chemical sensitization, cancers, and other health effects. Chemical sensitization and cancers are two disease endpoints of special interest in part because of the more abundant evidence on these occupational diseases in painters, and the fact that such diseases can occur at low concentrations of the putative chemical, and thus driving regulatory and disease prevention efforts. The "other" health effects group is intended to highlight other known or potential occupational diseases based on evidence from occupational medicine, epidemiology or chemical toxicity profiles.

3.4.1 | Respiratory and Dermal Sensitization

One of the most frequently reported adverse health effect of reactive chemical systems in the published literature is allergic sensitization that underpins occupational asthma and ACD from chemical sensitizers. Table 2 reports the list of sensitizers identified based on GHS classification and sensitization potency derived from evidence on human health studies and the local lymph node assay [27, 57]. We identified 14 sensitizers in Part B consisting of 9 amine hardeners, 4 solvents, and 1 nanofiller (Table 2). Most of them are listed as Class 1, 1 A and 1B according to the GHS classification. Definitions of these categories are provided in the footnote of Table 2. Based on the local lymph node assay (Table 2, skin potency category column), PAMAM and TETA have high sensitization potency, whereas Tris-DMP and TESPA have low to moderate sensitization potency. None of the chemicals listed in Table 2 has a "skin notation" designation.

Numerous occupational health studies and patch testing have documented dermatitis among workers exposed to epoxy resin systems including hardeners, dating back to 1977. Exposures to TETA used as a curing agent in aircraft painting were associated with asthma of a 54-year-old worker in a case report study. Severe asthma symptoms re-occurred once the patient returned to work, but the symptoms subsided once the company stopped using TETA [18]. Another case study of a 47-year-old worker developed non-atopic dermatitis from a two-component epoxy paint containing tris-DMP [58]. A clinical study of six patients exposed to 1,3-benzenedimethanamine documents eyelid and facial eczema represented as ACD [59]. Several high-quality studies from Finland have reported cases of ACD in workers exposed to amine hardeners, in addition to the better-known epoxy resins and isocyanates [32–35, 60, 61]. Among the Finnish construction painters, exposure to solvent-based epoxy resin systems was associated with higher rates of asthma-like symptoms, asthma, rhinitis, and chronic bronchitis compared to carpenters [62].

The literature on sensitization from epoxy resin systems often lists the copresence of isophorone diamine (IPDA), 4,4'-methylenedianiline (MDA), and *meta*-xylylene diamine (*m*-XDA) as Class I, strong sensitizers. Although these amine hardeners were not listed in the SDS of NEPCOAT products, they should be considered as part of the panel of analytes to measure and test in patch testing when investigating amine hardeners in epoxy-based coatings, and their absence in such products should be verified by independent chemical analysis.

Animal studies in the recent two decades have been used to assess the sensitization potency of various chemicals via the local lymph node assay and established the so-called effective concentration threshold (or EC3, concentration at which a stimulation index of 3 or more is achieved) [63]. Because of these more affordable and high throughput tests, reliable data are available for most sensitizers. Many amines share a common feature of being strong irritants to the eyes, upper airways, and the skin. TETA, the better studied amine, has been associated with dermal irritation and sensitization in vivo and in vitro assays, in addition to other health effects [64–68]. An animal toxicity study on exposure to DACH has been reported to cause skin irritation with clinical presentation of erythema, edema, delayed hypersensitivity, and necrosis at varied concentrations [69]. Other chemicals in Table 2, like solvents and wollastonite, have also been categorized as skin sensitizers.

A notable gap in the current occupational health literature is the lack of surveillance data on worker sensitization and other potential health effects, including asthma, in construction [27, 57] and limited literature on the inhalation toxicology of many of these chemical sensitizers.

3.4.2 | Cancer

Cancer is a major disease endpoint of great concern in part because the profession of industrial painter was classified by IARC as a Group 1 human carcinogen; however, the exact carcinogens are poorly documented. In our review, we identified nine Part B chemicals in NEPCOAT products that have

TABLE 2 | Skin and respiratory sensitizers identified in industrial metal structure coating systems.

Nr.	Chemicals	Chemical group	CAS number	Site/organ	Skin potency category[a]	GHS classification[b]	References	Layer[c]
1	Bis(pentamethyl-4-piperidyl) sebacate/ Bis(1,2,2,6,6-pentamethyl-4-piperidyl) sebacate	Amine hardener	41556-26-7	Skin	NA	Skin sensitization. 1A	ECHA,[d] PubChem[e]	T
2	Polyamidoamine (PAMAM)	Amine hardener	68082-29-1	Skin	HS	Skin sensitization.1A	ECHA, PubChem, IVDK [27], and DGUV [57].	P, M
3	2,4,6-Tris(dimethylaminomethyl) phenol (Tris-DMP)	Amine hardener	90-72-2	Skin	GMS	NA	RøMyhr et al. [32], Aalto-Korte et al. [33], Kanerva et al. [58], IVDK[f] [27], DGUV[g] [57].	P, M
4	Pentamethyl piperidyl sebacate/Methyl 1,2,2,6,6-pentamethyl-4-piperidyl sebacate	Amine hardener	82919-37-7	Skin	NA	Skin sensitization. 1	ECHA, PubChem	T
5	1,2-Diamino cyclohexane (DACH)	Amine hardener	694-83-7	Skin	NA	Skin sensitization. 1A	ECHA, PubChem	P, M
6	Triethylene tetramine (TETA)	Amine hardener	112-24-3	Skin	HS	Skin sensitization. 1	ECHA, PubChem, IVDK [27], DGUV [57].	P, M
7	Triethoxysilyl propylamine/(3-aminopropyl)triethoxysilane (TESPA)	Amine hardener	919-30-2	Skin	GMS	Skin sensitization. 1	ECHA, PubChem, IVDK [27], DGUV [57].	T
8	Fatty Acid Amine (FAA)	Amine hardener	85711-55-3	Skin	NA	Skin sensitization. 1A	ECHA, PubChem	P, M
9	Polyamide (PAmD)	Amine hardener	68410-23-1	Skin	U	Skin sensitization. 1A	ECHA, PubChem, IVDK [27], DGUV [57]	M
10	4-Morpholinecarboxaldehyde	Solvent	4394-85-8	Skin	NA	Skin sensitization.1B	ECHA, PubChem	T
11	Polycarboxylic acid ester	Solvent	91001-64-8	Skin	NA	Skin sensitization. 1	ECHA, PubChem	P
12	Dibutyltin bis (2,4-pentadionate)/ Dibutyltin bis(acetylacetonate)	Solvent	22673-19-4	Skin	NA	Skin sensitization.1	ECHA, PubChem	P

(Continues)

TABLE 2 | (Continued)

Nr.	Chemicals	Chemical group	CAS number	Site/organ	Skin potency category[a]	GHS classification[b]	References	Layer[c]
13	Dibutyltin dilaurate	Solvent	77-58-7	Skin	NA	Skin sensitization. 1	ECHA, PubChem	P
14	Wollastonite	Nanomaterial	13983-17-0	Respiratory	NA	Respiratory sensitization. 1	ECHA, PubChem	T

Note: Isophorone diamine (IPDA, CAS# 2855-13-2), 4,4'-methylene diamine (MDA, CAS# 101-77-9), and *meta*-xylylene diamine (*m*-XDA, CAS# 1477-55-0) were not reported in our reviewed NEPCOAT products. These amines are Class I potent sensitizers that appear often in other epoxy-based construction products, such as glues, and should be kept in mind when investigating amine hardeners in epoxy-based coatings.

Abbreviation: NA, not available.

[a]Skin potency category derived from evidence found from human health studies and the local lymph node assay [27, 57]. GMS – low or moderate sensitizing potency; HS – High sensitizing potency; HS → SHS = High sensitizing potency with limited data indicating tendency of chemical to be of very high sensitizing potency; U – unknown sensitizing potency; U → GMS – unknown sensitizing potency with limited data indicating tendency of chemical to be of low sensitizing potency; U → HS – unknown sensitizing potency with limited data indicating tendency of chemical to be of high sensitizing potency.

[b]Globally harmonized system (GHS) classification [28]. Skin sensitization category 1.1 A, 1B—may cause skin sensitization. Respiratory sensitization category 1, 1 A, 1B—may cause allergy or asthma symptoms or breathing difficulties if inhaled. Category 1 if: "(a) there is evidence in humans that the chemical can lead to specific hypersensitivity; and/or (b) if there are positive results from an appropriate animal test" If required, and if there are sufficient data, chemicals can be further categorized in subcategory 1 A and subcategory 1B. Category 1 A chemicals "show a high frequency of occurrence in humans; or a probability of occurrence of a high sensitization rate in humans based on animal or other tests". Category 1B chemicals "show a low to moderate frequency of occurrence in humans; or a probability of occurrence of a low to moderate sensitization rate in humans based on animal or other tests."

[c]Coating layer: M = mid-coat; P = primer, T = top-coat.

[d]European Chemical Agency (ECHA) chemical database [29].

[e]National Library of Medicine PubChem database [24].

[f]IVDK Information Network of Departments of Dermatology in Germany [27].

[g]German Social Accident Insurance [57].

been classified as IARC Group I (known) or Group IIB (possible) human carcinogens by IARC [70] (Table 3). Crystalline silica and ethanol, commonly used in coating and paint formulations, are classified as Group I carcinogen by IARC. The list of compounds in Group 2B, possibly carcinogenic to humans, includes titanium dioxide, 4-chlorobenzotrifluoride, carbon black, naphthalene, ethyl benzene, methyl isobutyl ketone, and cumene. The association between gastric cancer and occupational exposure to aromatic amines was examined in an analysis of 11 studies from the stomach cancer pooling project (StoP) reporting an increased rate of intestinal cancers with an OR 1.83 (95% CI 1.09–3.06) [71]. An epidemiological study demonstrated that workers exposed to respirable TiO_2 dust from six European countries had a higher incidence of lung cancer than the general population [72].

Carcinogenicity from solvent exposures is well documented. Occupational exposure to organic solvents used in paints has been associated with bladder tumors, multiple myeloma, and kidney and other urothelial tumors in spray painters [73]. Evidence of carcinogenicity from MIK, which is based on increased renal tubule neoplasms, mononuclear cell leukemia, and liver neoplasms in animals, has been reported by the National Toxicology Program (NTP) [74]. In vivo and in vitro studies point to the ability of toluene to promote cancer and genotoxicity [75–77].

3.4.3 | Other Possible Adverse Health Effects Associated With Part B Ingredients in Coating Products

Several other occupational diseases have been documented from epidemiological studies in industrial painters and the toxicity profile of ingredients identified in coating formulations, as summarized in Table 4. This section is not intended to be a detailed analysis of all other diseases and chemical-induced injury—as this would require a comprehensive review on its own—but rather as a reminder of other potentially serious diseases that can develop in painters. This list includes neurotoxicity (central or peripheral neuropathy related to multiple solvents), hepatotoxicity (fatty liver disease and fibrosis from several solvents and refractory particles), acute and chronic kidney injury (nephropathies from multiple solvents and metals), developmental and reproductive toxicity (solvents), ototoxicity (chemical-induced hearing loss from select solvents), as well as restrictive lung diseases from exposure to refractory materials such as crystalline silica and titanium dioxide (e.g., silicosis and fibrosis).

Neurotoxicity in construction painters has been documented extensively by numerous studies of the 1980 and 1990s. Exposure to the aromatic solvents, such as the BTEX mixture (benzene, toluene, ethylbenzene, xylenes) and mineral spirits, can cause peripheral neuropathy, structural central nervous system damage, neurobehavioral effects, impaired intellectual function, and more severe irreversible symptoms such as dementia, as documented by several studies [43, 49, 50, 80, 89]. Construction painters are at high risk for neuropsychiatric disability (OR = 1.47; 95% CI 1.07–2.02) [90]. Neurotoxicity could also result from inhaled particulate matter such as nano-sized TiO_2—due to oxidative stress and inflammation—outcomes that have been observed in the neurons of hippocampus,

TABLE 3 | Carcinogens identified in Part B of coating systems according to the IARC classification.

Nr.	Chemicals by group	CAS number	IARC classification[a]	Type of cancer[b]
1	Methyl isobutyl ketone	108-10-1	Group 2B (IARC monographs 101, 2013)	Liver and kidney
2	Ethyl benzene	100-51-6	Group 2B (IARC monographs 77, 2000)	Lung and liver
3	Naphthalene	91-20-3	Group 2B (IARC monographs 82, 2002)	Kidney, olfactory neuroblastoma, and lung
4	Ethanol	64-17-5	Group 1 (IARC monographs 96, 2012)	Oral cavity, pharynx, larynx, esophagus, liver, colorectum, and female breast
5	4-Chlorobenzotrifluoride	98-56-6	Group 2B (IARC monographs 125, 2020)	Lung, liver, and thyroid
6	Cumene	98-82-8	Group 2B (IARC monographs 101, 2013)	Liver, lung, and kidney
7	Crystalline Silica	14808-60-7	Group 1 (IARC monographs Sup[c] 7 68, 100C, 2012)	Lung, esophagus, stomach, and kidney
8	Titanium dioxide	13463-67-7	Group 2B (IARC monographs 93, 2010)	Lung
9	Carbon black	1333-86-4	Group 2B (IARC monographs 93, 2010)	Lung

[a]International Agency for Research on Cancer (IARC) classification [70]:
Group 1—Carcinogens to humans;
Group 2A—Probably carcinogenic to humans;
Group 2B—Possibly carcinogenic to humans;
Group 3—Not classifiable as to its carcinogenicity to humans.
[b]The type of cancer has been determined based on human and animal studies included in the IARC monographs.
[c]Sup = supplemental.

cerebellum, and subependymal area, together with reduction of neuroblast proliferation in rats and increased blood–brain barrier permeability to nanoparticles due to the damage of the blood–brain barrier [84, 85].

Solvents have been associated with chronic kidney disease affecting renal function, occurrence of proteinuria, and glomerulonephritis in painters in a meta-analysis study [81]. Extensive research on the health effects of solvents has also documented developmental toxicity [91], oxidative stress [77], and reproductive toxicity (Table 4). Methylene chloride, dimethyl formamide (DMF), dimethyl sulfoxide (DMSO), and *N*-methyl-2-pyrrolidone (NMP)—solvents with a high toxicity profile and high skin permeability coefficients—are still encountered in some industrial painting job sites. Inhalation exposure to several other glycol ethers (e.g., ethylene glycol monomethyl ether) used in coatings and paints, but not listed in the NEPCOAT products SDSs reviewed here, have been associated with congenital malformations, impaired spermatogenesis, and disturbed hematopoiesis in monkeys and rabbits [92], and percutaneous toxicity (erythema, edema, necrosis, and ecchymosis or skin discoloration) in rats [93].

Early signs of ototoxicity have been reported from exposure to aromatic solvents [78]. Ototoxicity is the functional impairment and cellular damage to the inner ear due to exposure to an ototoxic chemical substance. The Nordic Expert Group has listed *p*-xylene, ethylbenzene, and toluene (Table 4) as ototoxic chemicals based on evidence from animal and human studies [79]. These known neurotoxins could injure the sensory cells and the peripheral nerve endings of the inner ear [79].

Inhalation exposure to TiO_2 nanosize particles, common in coating formulations, can cause inflammation, cytotoxicity, and cell apoptosis [11, 86]. A cross-sectional study of 83 workers in a nano-TiO_2 manufacturing plant found significant association of oxidative stress, inflammation markers, lung damage markers, cardiovascular disease markers with occupational exposure to nano-TiO_2 [83]. In vivo animal studies on exposure to TiO_2 nanoparticles have shown oxidative stress due to an increased production of reactive oxygen species (ROS) as an important mechanism responsible for adverse effects in the respiratory and cardiovascular system [87, 88]. Morphological and physiological alterations in the kidneys following exposure to TiO_2 have also been reported [94]. In addition, workplace inhalation exposure to nanoscale and microscopic crystalline silica has also been associated with kidney toxicity and autoimmune disorders (Table 4) [82, 95].

The lack of contemporary longitudinal occupational epidemiology studies on industrial painters makes it difficult to gauge their disease severity and progression rates as well as the prevalence and incidence of these diseases.

4 | Discussion

In this review and synthesis, we document the composition of coating products approved by NEPCOAT for use in bridge painting in six New England states. We collected data on the frequency of appearance of each chemical in products and the content in the bulk product as reported by product SDSs. We

TABLE 4 | Existing occupational exposure limits and other health effects of Part B ingredients.

Chemicals by group	CAS number	NIOSH REL[a]	OSHA PEL[b]	ACGIH TLV[c]	Other health endpoints	References for health endpoints
Amines						
Triethylene tetramine	112-24-3	NA	NA	NA	Developmental toxicity Teratogenesis Genotoxicity	Korhenen et al. [64], Rochelle et al. [65], Cohen et al. [68], Leung [66]
Solvents						
Methyl *N*-amyl ketone Methyl ethyl ketone Methyl isobutyl ketone	110-43-0 78-93-3 108-10-1	TWA 100 ppm (465 mg/m^3) TWA 200 ppm (590 mg/m^3) ST 300 ppm (885 mg/m^3) TWA 50 ppm (205 mg/m^3) ST 75 ppm (300)	TWA 100 ppm (465 mg/m^3) TWA 200 ppm (590 mg/m^3) TWA 100 ppm (410 mg/m^3)	TWA 50 ppm (233) TWA 75 ppm STEL 150 ppm TWA 20 ppm (82 mg/m^3) STEL 75 ppm (307 mg/m^3)	Hepatotoxicity	PubChem,[d] ECHA[e]
Ethyl benzene Benzyl alcohol	100-41-4 100-51-6	TWA 100 ppm (435 mg/m^3) ST 125 ppm (545 mg/m^3)	TWA 100 ppm (435 mg/m^3)	TWA 20 ppm	Neurotoxicity Ototoxicity	Lee et al. [50], Pollastrini et al. 1994 [78], The Nordic Expert Group [79]
Xylene, mixed isomers	1330-20-7 108-38-3 106-42-3	TWA 100 ppm (435 mg/m^3) ST 150 ppm (655 mg/m^3)	TWA 100 ppm (435 mg/m^3)	TWA 20 ppm	Neurotoxicity Reproductive toxicity Kidney toxicity Gastrointestinal injury Ototoxicity	NIOSH [80], Jang et al. [48], Lee et al. [50], Lim et al. 2023 [81], The Nordic Expert Group [79]
Toluene	108-88-3	TWA 100 ppm (375 mg/m^3) ST 150 ppm (560 mg/m^3)	TWA 200 ppm	TWA 20 ppm	Neurotoxicity Genotoxicity Kidney toxicity Ototoxicity	NIOSH [80], Jang et al. [48] Tokunga et al. [77], Lim et al. [81], The Nordic Expert Group [79]
1,3,5-Trimethylbenzene 1,2,4-Trimethylbenzene 1,2,3-Trimethylbenzene	108-67-8 95-63-6 526-73-8	TWA 25 ppm (125 mg/m^3)	None	NA	Neurotoxicity	PubChem, ECHA
N-butyl acetate, *t*-Butyl acetate	123-86-4 540-88-5	TWA 150 ppm (710 mg/m^3)	TWA 150 ppm (710 mg/m^3)	TWA 50 ppm (238 mg/m^3)	Neurotoxicity Hepatotoxicity	PubChem, ECHA

(Continues)

TABLE 4 | (Continued)

Chemicals by group	CAS number	NIOSH REL[a]	OSHA PEL[b]	ACGIH TLV[c]	Other health endpoints	References for health endpoints
		ST 200 ppm (950 mg/m^3) TWA 200 ppm (950 mg/m^3)	TWA 200 ppm (950 mg/m^3)	STEL 150 ppm (712 mg/m^3)		
Isopropanol	67-63-0	TWA 400 ppm (980 mg/m^3) ST 500 ppm (1225 mg/m^3)	TWA 400 ppm (980 mg/m^3)	NA	Neurotoxicity	PubChem, ECHA
Ethanol	64-17-5	TWA 1000 ppm (1900 mg/m^3)	TWA 1000 ppm (1900 mg/m^3)	TLV-STEL 1000 ppm (1880 mg/m^3)	Neurotoxicity	PubChem, ECHA
1-Methoxy-2-Propyl Acetate	108-65-6	NA	NA	NA	Neurotoxicity	PubChem
1,2-Benzenedicarboxylic acid, di-C9-11-branched and linear alkyl esters	68515-43-5	NA	NA	NA	Hepatotoxicity	PubChem, ECHA
Dipropylene glycol methyl ether/(2-methoxymethylethoxy) propanol	34590-94-8	TWA 100 ppm (600 mg/m^3) ST 150 ppm (900 mg/m^3)	TWA 100 ppm (600 mg/m^3)	TWA 50 ppm	Neurotoxicity observed at high doses	PubChem, ECHA
2-Butoxyethanol	111-76-2	TWA 5 ppm (24 mg/m^3)	TWA 50 ppm (240 mg/m^3)	TWA 20 ppm (97 mg/m^3)	Neurotoxicity Hepatotoxicity	PubChem, ECHA
Propylene glycol monomethyl ether	107-98-2	TWA 100 ppm (360 mg/m^3) ST 150 ppm (540 mg/m^3)	None		Neurotoxicity	PubChem, ECHA
Methanol	67-56-1	TWA 200 ppm (260 mg/m^3) ST 250 ppm (325 mg/m^3)	TWA 200 ppm (260 mg/m^3)		Neurotoxicity Reproductive toxicity	PubChem, ECHA
Cumene (isopropyl benzene)	98-82-8	TWA 50 ppm (245 mg/m^3)	TWA 50 ppm (245 mg/m^3)	TWA 5 ppm (25 mg/m^3)	Neurotoxicity Hepatotoxicity	PubChem, ECHA

(Continues)

TABLE 4 | (Continued)

Chemicals by group	CAS number	NIOSH REL[a]	OSHA PEL[b]	ACGIH TLV[c]	Other health endpoints	References for health endpoints
Nano/materials additives						
Crystalline silica, respirable or non-respirable powder/quartz/ microcrystalline silica	14808-60-7	California: TWA 0.05 mg/m³	TWA 50 μg/m³	TWA 0.025 mg/m³, Rpm	Silicosis Chronic obstructive pulmonary disease Kidney toxicity	OSHA (2017) [95], PubChem
Titanium dioxide (anatase/ rutile) micro- or nanoform	13463-67-7 1317-80-2	TWA 2.4 mg/m³ (fine) TWA 0.3 mg/m³ (ultrafine)	TWA 15 mg/m³	TWA 0.2 rpm (nanoscale) TWA 2.5 rpm (fine-scale)	Kidney toxicity Genotoxicity Cardiovascular toxicity Neurotoxicity Lung fibroses	Zhao et al. 2018 [83], Valentini et al. 2018 [84], Zeman et al. 2018 [85], IARC 2012 [11], Jaishankar et al. 2014 [86], Grande et al. 2016 [87], Baranowska-Wójcik et al. 2020 [88]
Amorphous Silica/Silica Gel	7631-86-9	TWA 6 mg/m³	TWA 20 mppcf (80 mg/m³/%SiO_2)	NA	Kidney toxicity Autoimmune disorders Silicosis (from impurities)	ATSDR 2019 [82]
Wollastonite	13983-17-0	NA	NA	NA	Pulmonary diseases	PubChem
Zinc (dust or fume)	7440-66-6	NA	NA	NA	Hepatotoxicity Metal fume fever	PubChem
Mica	12001-26-2	TWA 3 mg/m³ (resp)	TWA 20 mppcf (mineral dust)	TWA 0.1 mg/m³, < 1% silica, respirable fraction	Pulmonary fibrosis	PubChem
Iron oxide	1309-37-1	TWA 5 mg/m³	TWA 10 mg/m³	TWA 5 mg/m³, Rpm	—	—
Ethyl silicate	78-10-4	TWA 10 ppm (85 mg/m³)	TWA 100 (850 mg/m³)	TWA 10 ppm (85 mg/m³)	Neurotoxicity Hepatotoxicity Kidney toxicity	PubChem
Zinc oxide	1314-13-2	TWA 5 mg/m³ (dust) TWA 5 mg/m³ (fume) ST 10 mg/m³ (fume)	TWA 5 mg/m³ (fume) TWA 15 mg/m³ (total dust) TWA 5 mg/m³ (resp dust)	TWA 2 mg/m³, Rpm STEL 10 mg/m³, Rpm	Metal fume fever	PubChem
Talc (hydrated magnesium silicate)	14807-96-6	TWA 2 mg/m³ (resp)	TWA 20 mppcf (mineral dust)	TWA 2 mg/m³, Rpm68	Pure talc has low toxicity. Possible contamination with	PubChem

(Continues)

TABLE 4 | (Continued)

Chemicals by group	CAS number	NIOSH REL[a]	OSHA PEL[b]	ACGIH TLV[c]	Other health endpoints	References for health endpoints
					asbestos fibers and other minerals increases the risk of mesothelioma and lung fibrosis. May interfere with Zn bioavailability and bone health.	

Note: Health effects reported are in addition to carcinogenicity and sensitization.
Abbreviations: NA, not available; Rpm, respirable particulate matter; ST/STEL, short term exposure limit; TWA, time weighted average.
[a]National Institute of Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) [25].
[b]Occupational Health and Safety (OSHA) Permissible Exposure Limit (PEL) [25].
[c]The American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) [26].
[d]PubChem—National Library of Medicine PubChem database [24].
[e]ECHA—European Chemical Agency (ECHA) chemical database [29].

document the complex chemistry of Part B mixtures and summarize the existing literature on exposures and health effects relevant to industrial coatings in construction. Painters' occupation that was classified as a carcinogen by IARC over three decades ago has received little attention by the occupational health community as documented by the limited available literature on the topic, with some exceptions, and the multiple data gaps on exposure and health outcomes.

The chemical cocktail that constitutes modern coatings includes 61 unique CAS numbers in Part B formulations, not including additional compounds present at less than 1% in the products that are not required to be reported in the SDS. These chemicals are delivered as a mixture of aerosols and vapors exposing workers via inhalation, ingestion, or skin contact. The presence of multiple powerful chemical sensitizers, carcinogens, neurotoxins, hepatotoxins, nephrotoxins, developmental toxins, and ototoxins, often in a single aerosol droplet, presents a sharp contrast between the exceptional performance of these formulations and their concerning toxicity profile. To reduce the gap between performance and safety profiles, a multiprong approach is needed. Among the many intervention opportunities that underpin the practice of occupational hygiene, we emphasize three pillars: product reformulation to reduce their intrinsic toxicity, problem recognition and health surveillance, and employing effective exposure controls.

Product reformulation and substitution of a toxic chemical with a safer and equally performing alternative is at the top of the hierarchy of controls. Although no good baseline data exist on the chemistry of these coating formulations from decades ago, we recognize that significant improvements have been made in product formulations over the years to reduce the volatility and toxicity of various solvents, isocyanate and epoxy formulations, as well as continued efforts by the manufacturers to replace isocyanates with safe non-isocyanate top-coats. Benzene, a class I human carcinogen, no longer is found in these paints, except as perhaps impurities in the supply chain. It is also understood that the high-performance standards that need to be met for these coatings place constraints in product formulations. Research on coating product reformulation that replaces some of the current toxic ingredients with safer and equally functional alternative compounds deserves a higher level of investment and more attention by federal agencies and the industry.

The Finnish occupational health model is a promising model to follow. The Finnish occupational health group has been testing various amine sensitizers in epoxy-based coating formulations and guiding their replacement with less sensitizing amine alternatives of equal performance profiles. This effort has been going hand-in-hand with their excellent medical surveillance efforts at the national level, which has enabled them to link occupational contact dermatitis and asthma with product chemistries. Sustainability in their research efforts over many decades is also a reminder that progress on chemical substitution requires prolonged research focus and sustained funding.

Medical surveillance is particularly important for a profession that faces such a complex set of health risks. Medical

surveillance, especially when sustained, saves many lives and is cost effective. For example, Ringen et al. (2022) document the positive impact of the medical screening program for construction and trade workers employed at US Department of Energy (DoE) nuclear site facilities through the Building Trades National Medical Screening (BTMed) program. Data from 25 years of surveillance estimated 32% reduction in chronic obstructive pulmonary disease (COPD), 48% in lung cancer mortality, 68% in all pneumoconiosis, 71% in pleural abnormalities, 35% in parenchymal abnormalities, but 20% reduction in hearing impairment [96]. This positive impact of medical surveillance in preventing illness and mortalities in construction trades at DoE sites was the greatest for agents and diseases that had regulatory incentives (e.g., asbestos, crystalline silica) and the least for hearing loss, for which the regulatory enforcement and incentives were weak. The importance of early detection of lung cancer and the need for continued medical screening were further reinforced in another analysis of (lung cancer) mortality rates among construction workers employed at DoE sites [97]. The World Trade Center Health Program and the longitudinal firefighter cancer cohort study based at University of Arizona and University of Miami are other relevant examples of models that could benefit construction painters [98, 99].

Industrial painters currently undergo biological and medical monitoring for lead exposure during abrasive blasting of old bridge paints (Code of federal regulations: 1926.62(j)(2) biological monitoring and 1926.62(j)(3) medical surveillance) [100]. This program could potentially be expanded to include additional agents of concern or disease endpoints, starting with chemical sensitizers and their diseases (ACD and chemically induced asthma) and cancers of the lungs and urinary bladder. The logistics of these programs are complex and need to be worked out.

Understanding and documenting exposures to toxic mixtures in industrial painters is a critical first step in identifying tasks and jobs with high exposures, in assessing adequacy of existing workplace exposure controls, in guiding and tracking exposure interventions, in enabling investigation of quantitative exposure–disease relationships, and in guiding policies. Lack of exposure and toxicity data for many of these chemicals of concern, as highlighted by this review, is a major barrier to disease prevention. As an illustration, for Class 1 amine sensitizers in Table 2 there are practically no exposure data, no occupational exposure standards or guidance values, and toxicity profiles by any exposure route are often not available. Table 2 and Supporting Information S1: Table S5 of amine hardeners in epoxy-based coatings have guided our own ongoing analytical and sampling method development and quantitative exposure assessment work.

In our previous work, we developed new sampling and analytical methods for personal exposure [23] and urinary biomonitoring of industrial painters to epoxy compounds [22], and documented significant uptake of Part A chemicals such as BADGE monomer through inhalation and dermal exposure while applying epoxy-based mid-coats [22], and high inhalation exposures to HDI-based aliphatic isocyanates while applying top-coats [9]. We also found that 38% (pre-shift) and 82% of (post-shift) urine samples of bridge painters had creatinine levels above the normal clinical value of 300 mg creatinine/dL, which later confirmed acute kidney injury through a panel of kidney injury biomarkers, such as KIM-1, osteopontin, clusterin, and NGAL [101]. Inadequate protective measures were consistently documented across multiple studies via urinary biomonitoring of epoxies [22] and isocyanates [9]. The existing workplace controls may not be protective against Part B exposures either and more investment in efforts towards exposure reduction should be a national priority for this construction sector.

In addition to chemical mixture exposures, we remain concerned about the compounding of chemical toxicity by working in hot environments which puts them at high risk for heat stroke, heat exhaustion, fainting, heat cramps, and electrolyte imbalance [102] that can further exacerbate chemical injury and compromise their physical safety. Mental health in construction trades has received a great deal of much deserved emphasis in recent years. However, missing from the discussion is the role of chemical exposures to neurotoxins and ototoxins in the construction workplace. Future research on construction painters needs to investigate the interplay of multiple stressors—mixed chemical exposures, heat stress, nutritional deficiencies and alike– because it is at the intersection of these domains of stressors where disease will likely develop first. We hope that this work will incentivize other research groups to study this complex problem and contribute to developing effective solutions.

5 | Conclusions

Painters working in metal structure coating activities, such as bridges, wind turbines, and elevated water tanks, can be exposed to a wide range of chemicals in mixtures of two-component isocyanate- and epoxy-based formulations (amine hardeners, solvents, nanofillers, and other additives), which contain several carcinogens and potent chemical sensitizers. Although painters were classified by IARC as a Group I (carcinogenic to humans) occupation since 1989, based on increased risks of lung and urinary bladder cancers, they may be at high risk for other types of cancers, as well as for skin and respiratory sensitization, asthma, COPD, lung fibrosis, neurotoxicity, hepatotoxicity, kidney toxicity, and ototoxicity. We argue for the need to develop a national multi-prong strategy to further document and reduce chemical exposures and health risks among construction painters. Increased awareness, exposure monitoring and control, medical surveillance and screening, and product reformulation are important initiatives that will help reduce the future burden of illnesses and reduce mortality in this construction trade.

Author Contributions

Paridhi Patel: literature review, product reviews, data curation, writing–original draft. **Dhimiter Bello:** conceptualization, project administration, resources, funding acquisition, writing–review and editing. **Anila Bello:** conceptualization, methodology, supervision, writing–review and editing.

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Disclosure

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John Meyer declares that he has no conflict of interest in the review and publication decision regarding this article.

Ethics Statement

This work was performed at the University of Massachusetts Lowell (UMass Lowell) as part of a larger project and was approved by the Institutional Review Board. The current work, however, does not involve interaction with human subjects.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.